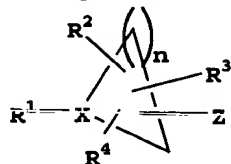


What is Claimed is:

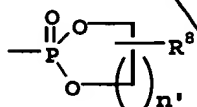
1. A compound having the structure



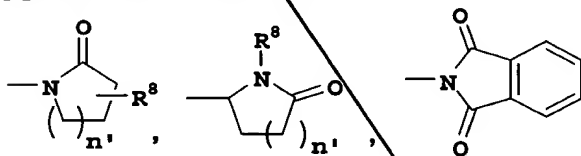
wherein n is an integer from 1 to 5;

- 5        X is N or C-R<sup>5</sup> wherein R<sup>5</sup> is H, halo, alkenyl, alkynyl, alkoxy, alkyl, aryl or heteroaryl;  
       Z is a heteroaryl group;  
       R<sup>1</sup> is H, alkyl, alkenyl, alkynyl, alkoxy, alkenyloxy, alkynyloxy, (alkyl or aryl)<sub>3</sub>Si (where each  
 10    alkyl or aryl group is independent), cycloalkyl, cycloalkenyl, amino, alkylamino, dialkylamino, alkenylamino, alkynylamino, arylalkylamino, aryl, arylalkyl, arylamino, aryloxy, cycloheteroalkyl, cycloheteroalkylalkyl, heteroaryl, heteroarylamino,  
 15    heteroaryloxy, arylthio, arylsulfinyl, arylsulfonyl, thio, alkylthio, alkylsulfinyl, alkylsulfonyl, heteroarylthio, heteroarylsulfinyl, heteroarylsulfonyl, halogen, haloalkyl, polyhaloalkyl, polyhaloalkoxy, aminothio, aminosulfinyl, aminosulfonyl,  
 20    alkylsulfonylamino, alkenylsulfonylamino, alkynylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, alkylaminocarbonyl, arylaminocarbonyl, heteroarylamino, hydroxy, acyl, carboxy, aminocarbonyl, alkylcarbonyl,  
 25    alkoxycarbonyl, alkylcarbonyloxy, alkylcarbonylamino, arylcarbonyl, arylcarbonyloxy, arylcarbonylamino, heteroarylcarbonyl, heteroarylcarbonyloxy, heteroarylcarbonylamino, cyano, nitro, alkenylcarbonylamino, alkynylcarbonylamino,  
 30    alkylaminocarbonylamino, alkenylaminocarbonylamino, alkynylaminocarbonylamino, arylaminocarbonylamino, heteroarylamino, alkoxycarbonylamino, alkenyloxycarbonylamino, alkynyloxycarbonylamino, aryloxycarbonylamino, heteroaryloxycarbonylamino,

aminocarbonylamino, alkylaminocarbonyloxy,  
alkoxycarbonylamino, 1,1-(alkoxyl or aryloxy)<sub>2</sub>alkyl  
(where the two aryl or alkyl substituents can be  
independently defined, or linked to one another to form a  
5 ring),  $S(O)_2R^6R^7$ ,  $-NR^6(C=NR^7)alkyl$ ,  $-NR^6(C=NR^7)alkenyl$ ,  
 $-NR^6(C=NR^7)alkynyl$ ,  $-NR^6(C=NR^7)heteroaryl$ ,  $-NR^8(C=NCN)-$   
amino,



pyridine-N-oxide,



10 (where Q is O or H<sub>2</sub> and n' is 0, 1, 2 or 3) or

$-C(=CH-CH_2-C(=O)-R^{8a})NR^8R^9$ ; tetrazolyl, pyrazolyl, pyridyl,  
thiazolyl, pyrimidinyl, imidazole, oxazole, or triazole,  
-PO(R<sup>13</sup>)(R<sup>14</sup>), (where R<sup>13</sup> and R<sup>14</sup> are independently alkyl,  
15 aryl, alkoxy, aryloxy, heteroaryl, heteroarylalkyl,  
heteroaryloxy, heteroarylalkoxy, cycloheteroalkyl,  
cycloheteroalkylalkyl, cycloheteroalkoxy, or  
cycloheteroalkylalkoxy);

20 R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup>, R<sup>8a</sup> and R<sup>9</sup> are the same or different and  
are independently hydrogen, alkyl, haloalkyl, aryl,  
heteroaryl, arylalkyl, cycloalkyl, (cycloalkyl)alkyl, or  
cycloheteroalkyl;

and R<sup>1</sup> may be optionally substituted with from one  
to five substituents;

25 R<sup>2</sup>, R<sup>3</sup> and R<sup>4</sup> are the same or different and are  
independently any of the groups set out for R<sup>1</sup> and may be  
optionally independently substituted with from one to  
five substituents, which may be the same or different;

including pharmaceutically acceptable salts  
30 thereof, prodrugs thereof, and all stereoisomers thereof;  
with the proviso that where X is N, n is 4, and Z is

*a' cont*  
 imidazol-4-yl or 5-alkylimidazol-4-yl attached at the 4-position of the ring, then  $R^1$  is other than phenyl or substituted phenyl.

*Sub G'*  
 2. The compound as defined in Claim 1 wherein Z is  
 5 a heteroaryl group containing 1 to 4 heteroatoms, at least one of which is a nitrogen atom, the heteroaryl group being attached to the rest of the molecule via an available nitrogen or carbon atom.

3. The compound as defined in Claim 1 wherein at  
 10 least one of  $R^1$ ,  $R^2$ ,  $R^3$  and  $R^4$  is aryl or heteroaryl.

4. The compound as defined in Claim 1 wherein X is N.

5. The compound as defined in Claim 1 wherein X is C- $R^5$ .

*005260-005260*  
 6. The compound as defined in Claim 1 wherein Z is  
 15 imidazole, aminoimidazole, alkylimidazole, alkylthioimidazole, alkylthio(amino)imidazole, amino-(alkyl)imidazole, oxazole, (alkanoylamino)imidazole, thiazole, benzimidazole, aminethiazole, aminooxazole,  
 20 aminooxadiazole, dialkylimidazole, alkyl(alkanoylamino)imidazole, alkyl(amino)imidazole, arylaminocarbonylamino(alkyl)imidazole, alkoxycarbonylamino(alkyl)imidazole, alkylcarbonylamino(alkyl)imidazole, aminotriazole or  
 25 diaminopyrimidine.

7. The compound as defined in Claim 1 wherein  $R^1$  is aryl or heteroaryl.

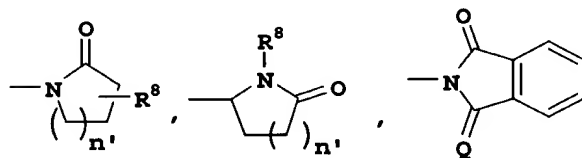
8. The compound as defined in Claim 1 wherein the  
 30  $R^1$  group may be substituted within from one to five of the following groups:

*Sub G'*  
 alkyl, alkenyl, alkynyl, alkoxy, alkenyloxy, alkynyloxy, (alkyl or aryl)<sub>3</sub>Si (where each alkyl or aryl group is independent), cycloalkyl, cycloalkenyl, amino, alkylamino, dialkylamino, alkenylamino, alkynylamino,  
 35 arylalkylamino, aryl, arylalkyl, arylamino, aryloxy, cycloheteroalkyl, cycloheteroalkylalkyl, heteroaryl, heteroarylamino, heteroaryloxy, arylthio, arylsulfinyl,

arylsulfonyl, thio, alkylthio, alkylsulfinyl,  
 alkylsulfonyl, heteroarylthio, heteroarylsulfinyl,  
 heteroarylsulfonyl, halogen, haloalkyl, polyhaloalkyl  
 such as  $\text{CF}_3$  and  $\text{CF}_3\text{CH}_2$ , polyhaloalkyloxy such as  $\text{CF}_3\text{O}$  and  
 5  $\text{CF}_3\text{CH}_2\text{O}$ , aminothio, aminosulfinyl, aminosulfonyl,  
 alkylsulfonylamino, alkenylsulfonylamino,  
 alkynylsulfonylamino, arylsulfonylamino,  
 heteroarylsulfonylamino, alkylaminocarbonyl,  
 arylaminocarbonyl, heteroarylaminocarbonyl, hydroxy,  
 10 acyl, carboxy, aminocarbonyl, alkylcarbonyl,  
 alkoxycarbonyl, alkylcarbonyloxy, alkylcarbonylamino,  
 arylcarbonyl, arylcarbonyloxy, arylcarbonylamino,  
 heteroarylcarbonyl, heteroarylcarbonyloxy,  
 heteroarylcarbonylamino, cyano, nitro,  
 15 alkenylcarbonylamino, alkynylcarbonylamino,  
 alkylaminocarbonylamino, alkenylaminocarbonylamino,  
 alkynylaminocarbonylamino, arylaminocarbonylamino,  
 heteroarylaminocarbonylamino, alkoxycarbonylamino,  
 alkenyloxycarbonylamino, alkynyloxycarbonylamino,  
 20 aryloxycarbonylamino, heteroaryloxycarbonylamino,  
 aminocarbonylamino, alkylaminocarbonyloxy, 1,1-(alkoxyl  
 or aryloxy)<sub>2</sub>alkyl (where the two aryl or alkyl  
 substituents can be independently defined, or linked to  
 one another to form a ring, such as 1,3-dioxane or 1,3-  
 25 dioxolane),  $\text{S}(\text{O})_2\text{R}^6\text{R}^7$ ,  $-\text{NR}^6(\text{C}=\text{NR}^7)\text{alkyl}$ ,

$\text{NR}^6(\text{C}=\text{NR}^7)\text{alkenyl}$ ,  $-\text{NR}^6(\text{C}=\text{NR}^7)\text{alkynyl}$ ,

$\text{NR}^6(\text{C}=\text{NR}^7)\text{heteroaryl}$ ,  $-\text{NR}^8(\text{C}=\text{NCN})\text{-amino}$ , pyridine-N-oxide,



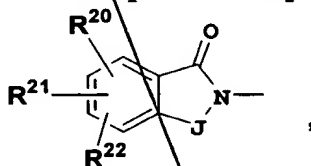
30

(where Q is O or  $\text{H}_2$  and  $n'$  is 0, 1, 2 or 3) or  $-\text{C}(\text{NR}^8\text{R}^9)=\text{CH}-\text{C}(=\text{O})-\text{R}^{8a}$ ;  
 tetrazolyl, pyrazolyl, pyridyl, thiazolyl, pyrimidinyl,

imidazole, oxazole or triazole;  $-PO(R^{13})(R^{14})$ , (where  $R^{13}$  and  $R^{14}$  are independently alkyl, aryl, alkoxy, aryloxy, heteroaryl, heteroarylalkyl, heteroaryloxy, heteroarylalkoxy, cycloheteroalkyl, cycloheteroalkylalkyl, cycloheteroalkoxy, or cycloheteroalkylalkoxy);

$R^6$ ,  $R^7$ ,  $R^8$ ,  $R^{8a}$  and  $R^9$  are independently hydrogen, alkyl, haloalkyl, aryl, heteroaryl, arylalkyl, cycloalkyl, (cycloalkyl)alkyl or cycloheteroalkyl, which substituents may be the same or different from each other and may be the same or different from the base  $R^1$  group.

9. The compound as defined in Claim 1 wherein  $R^1$  is substituted with one to five of the following substituents: alkyl, alkylaminocarbonyl, arylaminocarbonyl, heteroarylaminocarbonyl, alkylcarbonylamino, heteroaryl, halo, aryl, cycloalkylcarbonylamino, arylcarbonylamino, heteroarylcarbonylamino, alkoxy carbonylamino, guanidiny, nitro, cycloheteroalkyl, aryloxy carbonylamino, heteroaryloxy carbonylamino, uriedo (where the uriedo nitrogens may be substituted with alkyl, aryl or heteroaryl), heterocyclylcarbonylamino (where the heterocycle is connected to the carbonyl group via a nitrogen or carbon atom), alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino,



Where J is:  $CHR^{23}$ ,  $\begin{array}{c} -C- \\ || \\ O \end{array}$ ,  $\begin{array}{c} -CH-CH- \\ | \quad | \\ R^{24} \quad R^{25} \end{array}$  or  $\begin{array}{c} -C=C- \\ | \quad | \\ R^{24} \quad R^{25} \end{array}$ ;

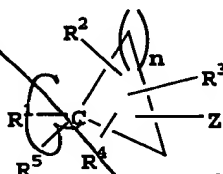
$R^{23}$ ,  $R^{24}$  and  $R^{25}$  are independently hydrogen, alkyl, alkenyl, alkynyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, cycloalkyl, or cycloalkylalkyl;

$R^{20}$ ,  $R^{21}$ ,  $R^{22}$  are independently hydrogen, halo, alkyl, alkenyl, alkoxy, aryloxy, aryl, arylalkyl, alkylmercapto, arylmercapto, cycloalkyl, cycloalkylalkyl,

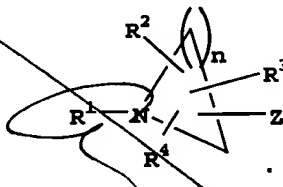
heteroaryl, heteroarylalkyl, hydroxy or haloalkyl; and these preferred substituents may either be directly attached to  $R^1$ , or attached via an alkylene chain at an open position, which substituents may be the same or different from each other and may be the same or different from the base  $R^1$  group.

- 5  
Sub  
G1
10. The compound as defined in Claim 1 wherein Z is imidazole, aminoimidazole, alkylimidazole, alkylthioimidazole, alkylthio(amino)imidazole, amino(alkyl)imidazole or (acetylamino)imidazole.

11. The compound as defined in Claim 1 having the formula

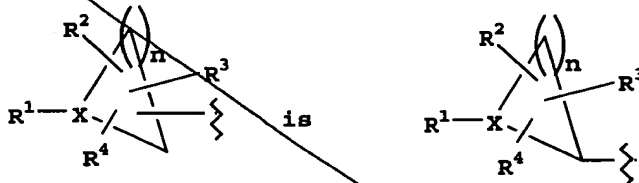


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005000 00203500
12. The compound as defined in Claim 1 having the formula



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13. The compound as defined in Claim 7 wherein  $R^1$  is aryl or heteroaryl and n is 1 or 4

14. The compound as defined in Claim 1 wherein the moiety



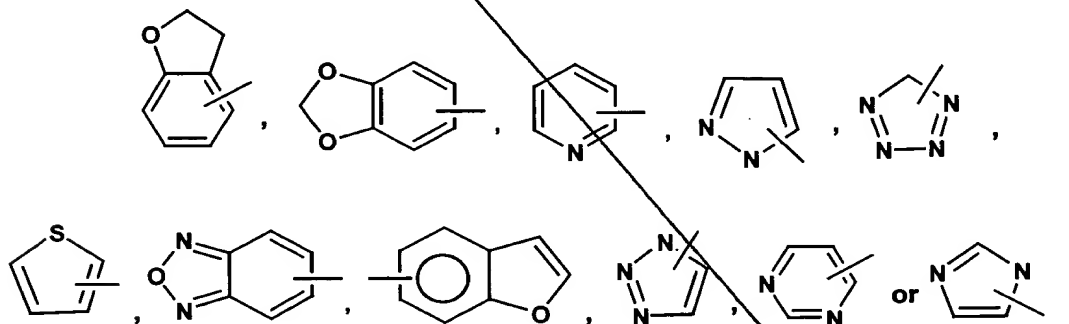
- 25  
Sub  
G1
15. The compound as defined in Claim 1 wherein  $R^2$  and  $R^3$  are independently H, lower alkyl, lower alkoxy or aryl, and  $R^4$  and  $R^5$  are each hydrogen.

16. The compound as defined in Claim 1 wherein n is 1 or 4.

17. The compound as defined in Claim 1 wherein n is 4, R<sup>2</sup> and R<sup>3</sup> are independently H or lower alkyl, and R<sup>4</sup> and R<sup>5</sup> are each H, and R<sup>1</sup> is aryl or heteroaryl.

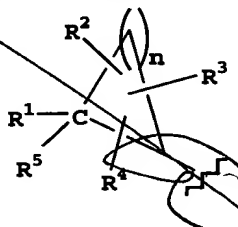
18. The compound as defined in Claim 1 wherein R<sup>1</sup> is phenyl, substituted phenyl or heteroaryl.

19. The compound as defined in Claim 1 wherein R<sup>1</sup> is phenyl, halophenyl, dihalophenyl, alkylphenyl, nitrophenyl, dialkoxyphenyl, alkoxy(halo)phenyl, alkoxyphenyl, halo(nitro)phenyl, trifluoromethylphenyl, biphenyl, heteroarylphenyl, cycloheteroalkylphenyl, alkylthiophenyl, trialkoxyphenyl or halo(dialkoxy)phenyl, phenylalkyl,

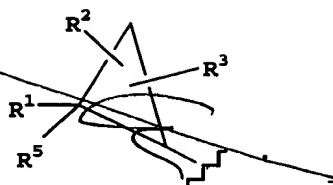


20. The compound as defined in Claim 1 wherein R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup> and/or R<sup>4</sup> may be joined together with the N atom and/or carbons to which they are attached to form a non-aromatic ring.

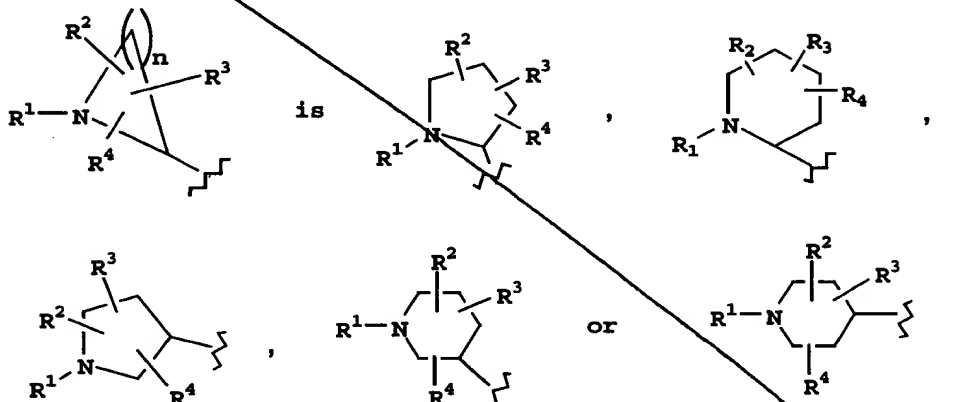
21. The compounds as defined in Claim 11 wherein



is



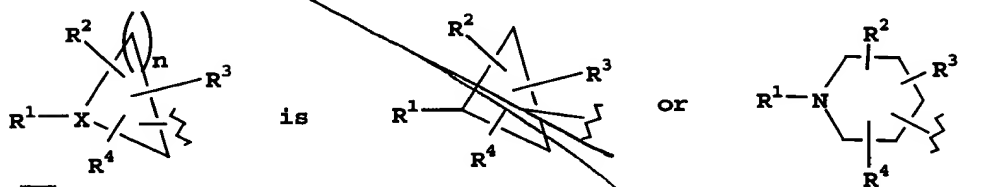
22. The compound as defined in Claim 1 wherein



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23. The compound as defined in Claim 1 wherein  $n$  is 1,  $X$  is CH,  $R^2$  and  $R^3$  are independently lower alkyl or H.

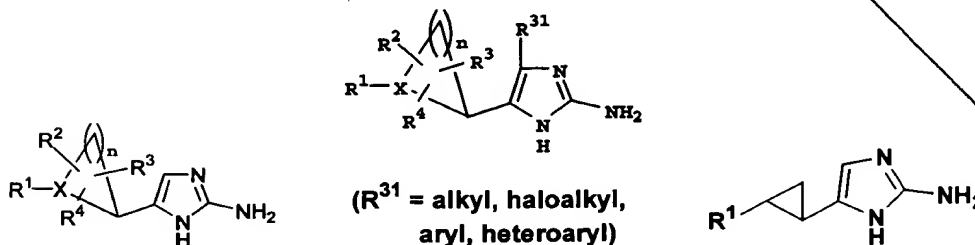
24. The compound as defined in Claim 1 wherein



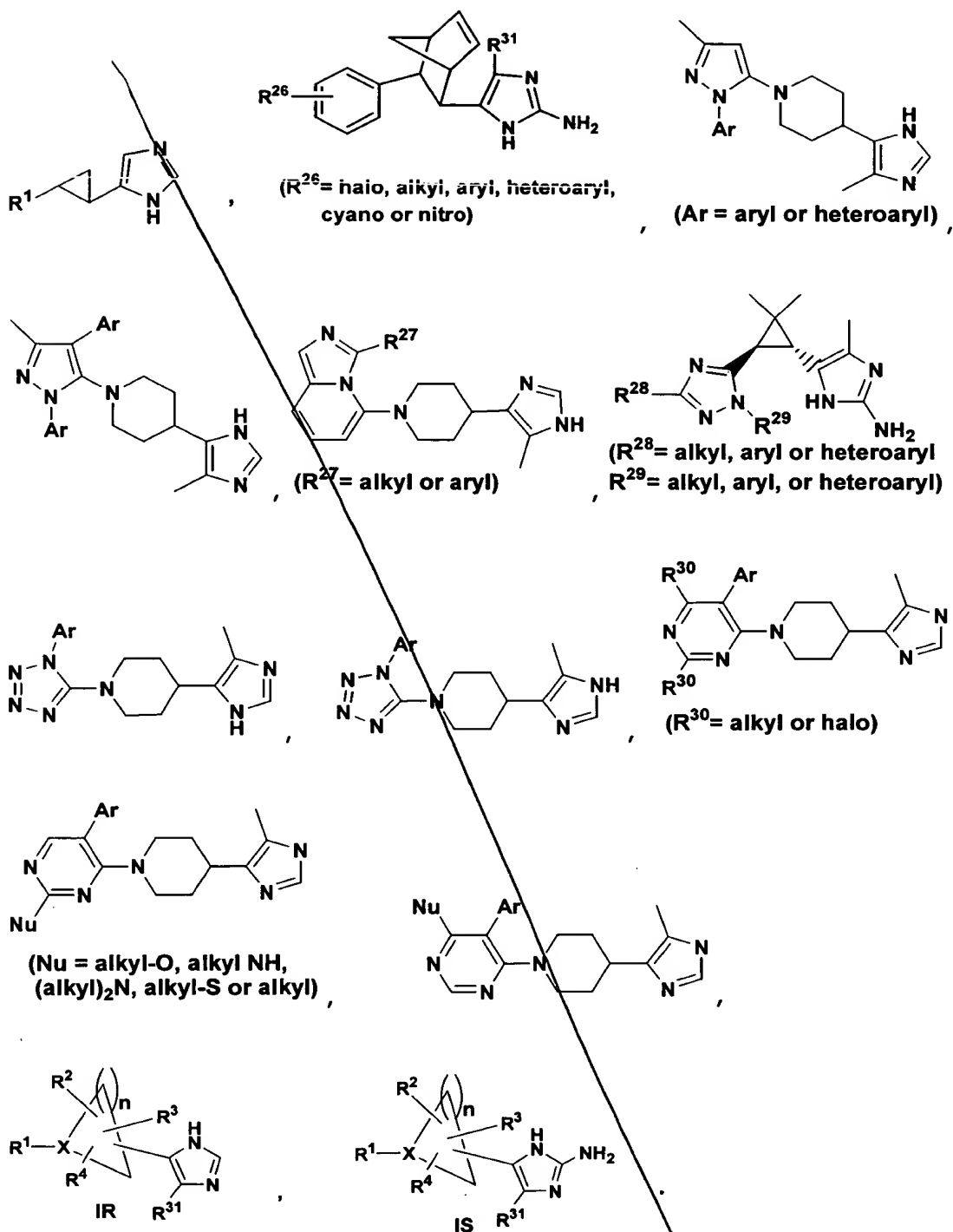
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25. The compound as defined in Claim 1 having the structure

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26. The compound as defined in Claim 1 wherein R<sup>1</sup> is 4-bromophenyl, 4-chlorophenyl, 3-bromophenyl, 3,5-dimethoxyphenyl, 4-methylphenyl, 2,4-dichlorophenyl, 3-nitrophenyl, 2-chlorophenyl, 3-chlorophenyl, 2,5-dimethylphenyl, 2-methylphenyl, 3-methylphenyl, 4-

methylphenyl, 2,3-dimethoxyphenyl, 4-trifluoromethyl-  
 phenyl, 3-trifluoromethoxyphenyl, 4-biphenyl, 2-bromo-  
 4,5-dimethoxyphenyl, 4-methylthiophenyl, 3,4,5-  
 trimethoxyphenyl, 4-fluorophenyl, 2-chloro-3,4-  
 5 dimethoxyphenyl, 4-nitrophenyl, benzyl, 3-methoxyphenyl,  
 4-methoxyphenyl, 2-methoxyphenyl, 3-bromo-4-fluorophenyl,  
 2-fluoro-5-methoxyphenyl, 3-chloro-4-nitrophenyl, 2-  
 fluoro-4-bromophenyl, 3-ethoxyphenyl, 3-  
 trifluoromethylphenyl, 3,5-difluorophenyl, 3,5-  
 10 dichlorophenyl, 3,5-bistrifluoromethylphenyl, 4-  
 fluorophenyl, 3-trifluorophenyl, 3-(N-pyrrolyl)phenyl, 3-  
 (N-pyrrolidinyl)phenyl, 3-(N-pyrazolinyl)phenyl, 3-(N-  
 imidazolyl)phenyl, phenyltetrazole, 1-(2,4-dihalo-5-  
 alkoxyphenyltetrazol-5-yl, alkylphenyltetrazole,  
 15 halophenyltetrazol, 1-(2-alkoxy-5-halophenyl)tetrazol-5-  
 yl, 1-(3-alkyl-4-halophenyl)tetrazol-5-yl,  
 alkoxyphenyltetrazole, alkyl(halo)phenyltetrazole,  
 alkoxy(halo)phenyltetrazole,  
 alkoxy(alkyl)(halo)phenyltetrazole,  
 20 phenyl-alkyl-pyrazole, alkoxyphenyl-alkyl-pyrazole,  
 halophenyl-alkyl-pyrazole, alkyl(halo)phenyl-alkyl-  
 pyrazole, alkylphenyl-alkyl-pyrazole, alkoxy(halo)phenyl-  
 alkyl-pyrazole, alkoxy(alkyl)phenyl-alkyl-pyrazole,  
 dihalophenyl-alkyl-pyrazole, dialkylphenyl-alkyl-  
 25 pyrazole, alkoxyphenyl-alkyl-pyrazole, halophenyl-  
 haloalkyl-pyrazole, alkoxyphenyl(alkyl)(halo)pyrazole,  
 phenylpyrimidine, phenyl(halo)pyrimidine,  
 diphenylpyrimidine, halophenyl(halo)pyrimidine,  
 dihalopyrimidine, diphenyl(halo)pyrimidine,  
 30 halo(phenyl)pyrimidine, dialkyl(halo)pyrimidine,  
 dihalophenylpyrimidine, alkylphenylpyrimidine,  
 alkoxyphenylpyrimidine, alkylphenyl(alkoxy)pyrimidine,  
 dialkylphenyl(alkoxy)pyrimidine,  
 alkyl(halo)phenyl(alkoxy)pyrimidine,  
 35 alkoxy(halo)phenyl(alkoxy)pyrimidine,  
 dihalophenyl(dialkylamino)pyrimidine,  
 heteroaryl(dihalophenyl)pyrimidine, halophenylpyrimidine,

Q5  
cont

\*C1=CC=C2C(=C1)N(C2)C3=CC=CC=C3

20            27. The compound as defined in Claim 1 wherein  
X is CH or N;

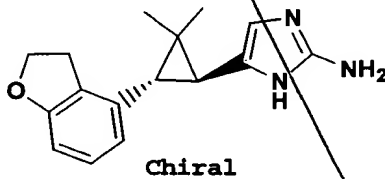
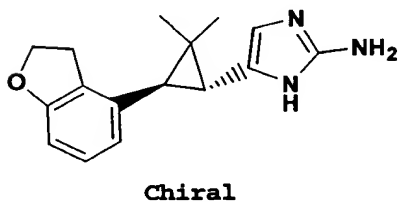
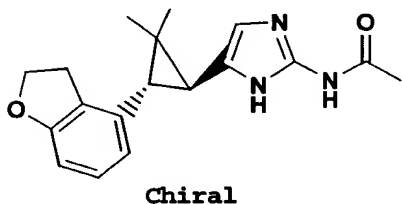
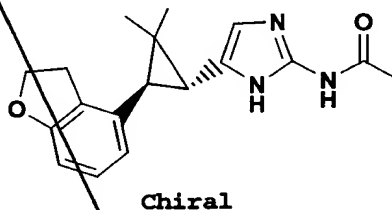
25  $R^4$  is  $H$ ;

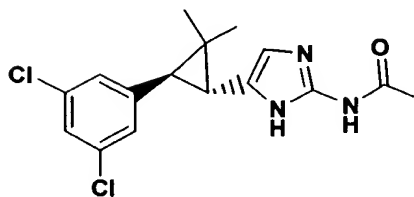
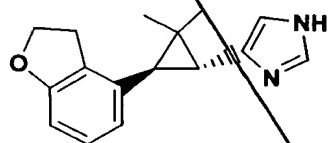
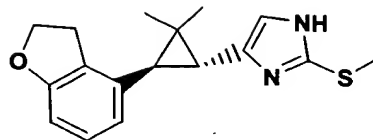
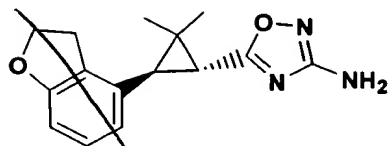
- 185 -

- Q5  
cont
- 1- (3-methylphenyl) tetrazol-5-yl,
  - 1- (2-chlorophenyl) tetrazol-5-yl,
  - 1- (2-methoxy-5-chloro) tetrazol-5-yl,
  - 2- (propylcarbonylamino) phenyl,
  - 5 1- (3-methyl-4-chlorophenyl) tetrazol-5-yl,
  - 1- (2-methoxy-5-chlorophenyl) tetrazol-5-yl,
  - 1- (3-methoxyphenyl) tetrazol-5-yl,
  - 1- (2-methoxy-5-chlorophenyl) tetrazol-5-yl,
  - 1- (3-chlorophenyl) -3-methylpyrazol-5-yl,
  - 10 1- (3-fluorophenyl) -3-methylpyrazol-5-yl,
  - 1- (3-methoxyphenyl) -3-methylpyrazol-5-yl,
  - 1- (3,5-dichlorophenyl) -3-methylpyrazol-5-yl,
  - 1- (3-chlorophenyl) -3-ethylpyrazol-5-yl,
  - 1- (3-chloro-4-methylphenyl) -3-methylpyrazol-5-yl,
  - 15 1- (2,4-dimethylphenyl) -3-methylpyrazol-5-yl,
  - 1- (3-chloro-4-fluorophenyl) -3-methylpyrazol-5-yl,
  - 1- (3-trifluoromethylphenyl) -3-methylpyrazol-5-yl,
  - 1- (3-chlorophenyl) -3-trifluoromethylpyrazol-5-yl,
  - 1- (3-methylphenyl) 3-methylpyrazol-5-yl,
  - 20 1- (3-chlorophenyl) -3-ethylpyrazol-5-yl,
  - 5- (3-chloro-4-fluorophenyl) pyrimidin-4-yl,
  - 5- (2-chlorophenyl) pyrimidin-4-yl,
  - 5- (3-methylphenyl) pyrimidin-4-yl,
  - 5- (3-trifluoromethylphenyl) pyrimidin-4-yl,
  - 25 5- (2,4-dichlorophenyl) pyrimidin-4-yl,
  - 5- (2,5-dimethylphenyl) pyrimidin-4-yl,
  - 5- (3,4-dichlorophenyl) pyrimidin-4-yl,
  - 5- (2,3-dimethylphenyl) pyrimidin-4-yl,
  - 5- (2-methoxy-5-chlorophenyl) pyrimidin-4-yl,
  - 30 5- (2-methoxy-5-fluorophenyl) pyrimidin-4-yl,
  - 5- (3-methyl-4-fluorophenyl) pyrimidin-4-yl,
  - 3- (3-methyl-4-fluorophenyl) pyridin-2-yl,
  - 3- (3-chloro-4-fluorophenyl) pyridin-2-yl,
  - 3- (3-trifluoromethoxyphenyl) pyridin-2-yl,
  - 35 5- (3-chloro-4-fluorophenyl) -2-methoxy-pyrimidin-4-yl,
  - 5- (3-chloro-4-fluorophenyl) -2-dimethylamino-pyrimidin-4-yl,

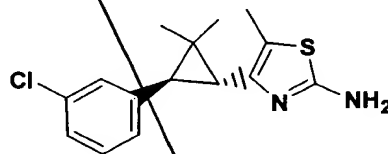
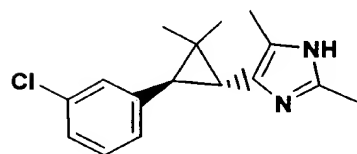
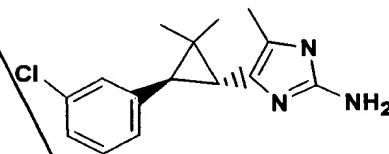
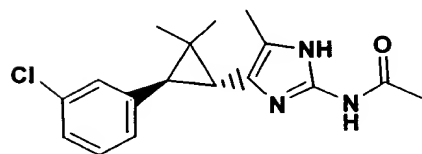
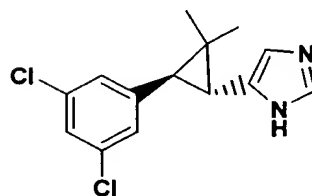
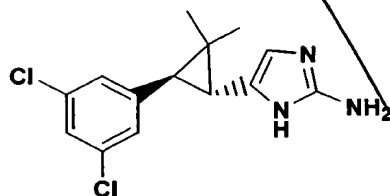
Q5  
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28. The compound as defined in Claim 1 having the  
20 strucutre

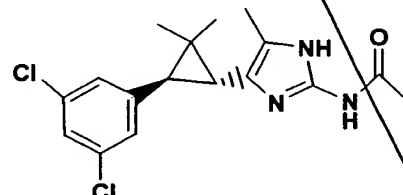
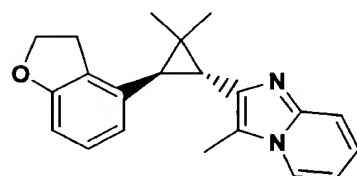
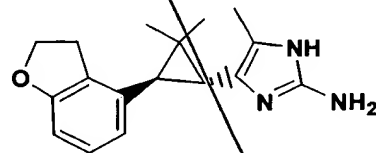
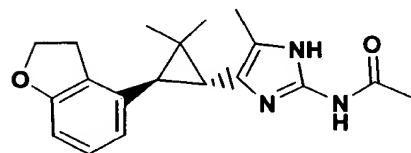


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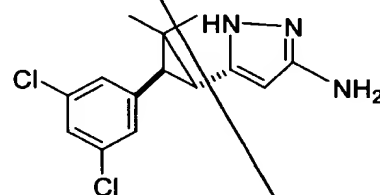
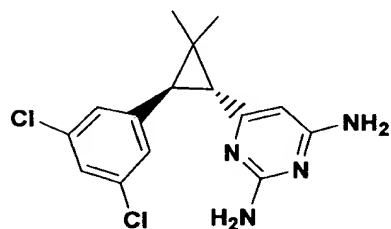
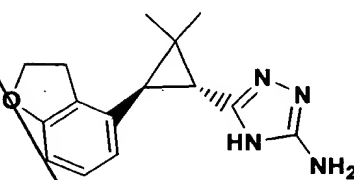
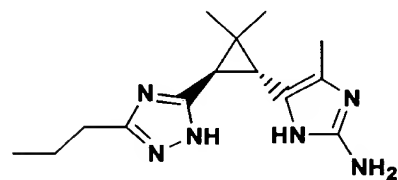
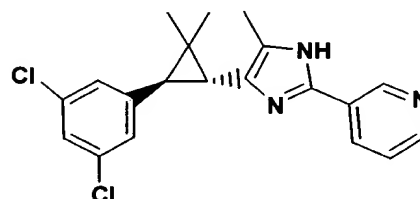
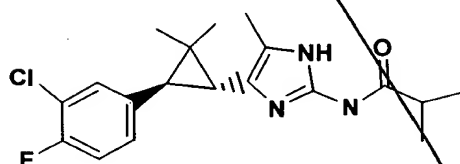
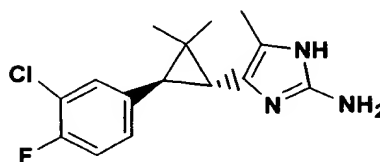
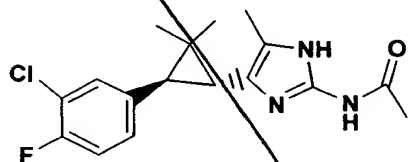
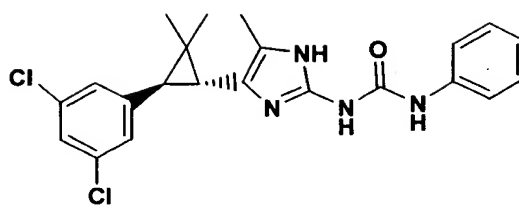
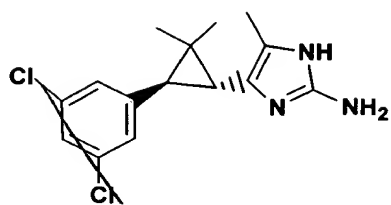
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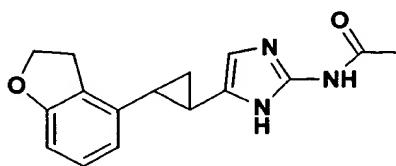
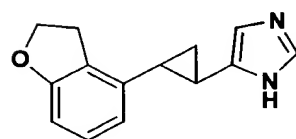
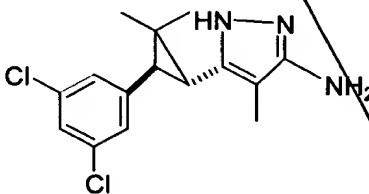
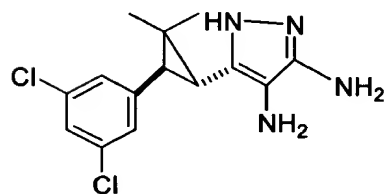
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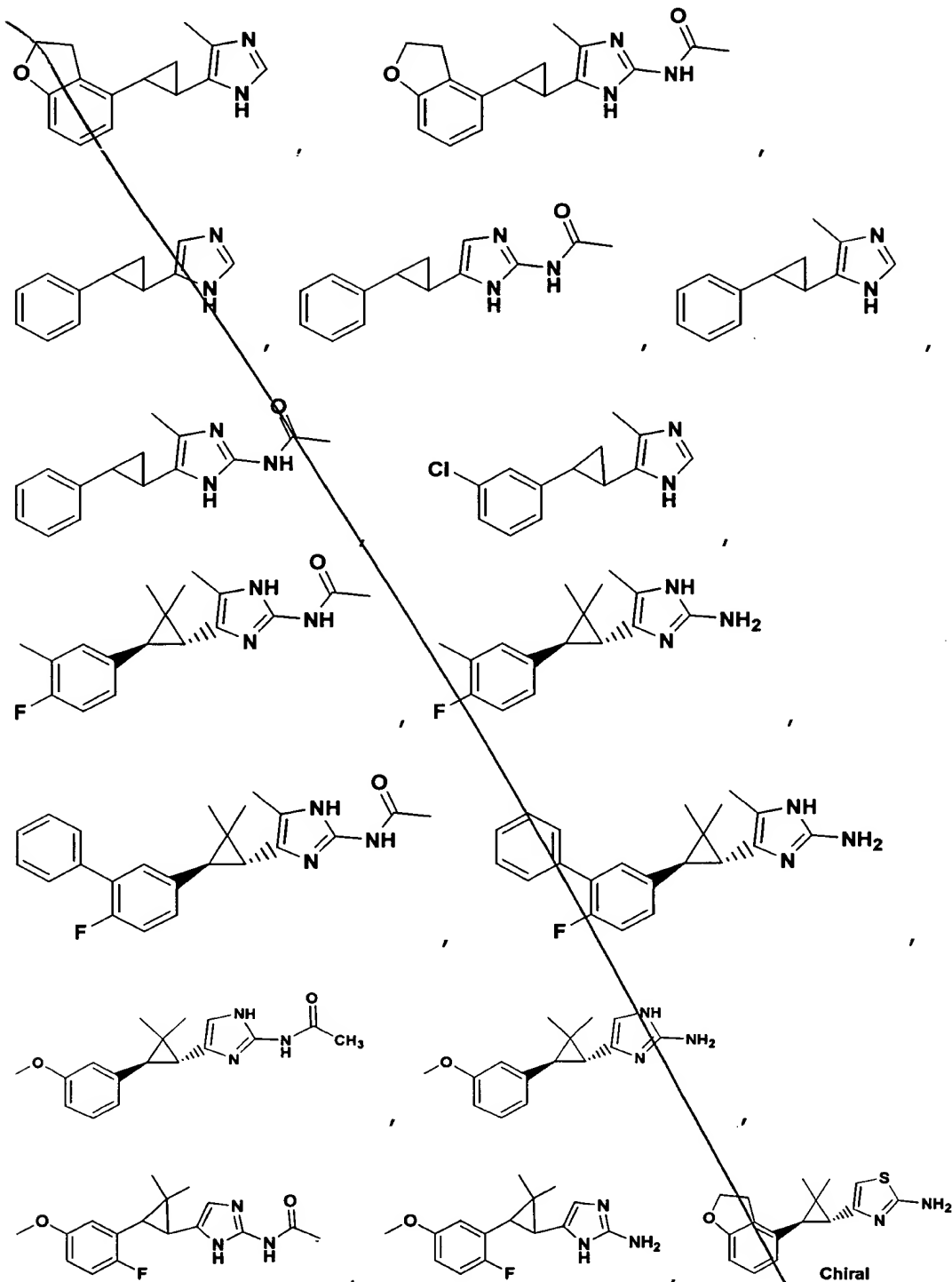
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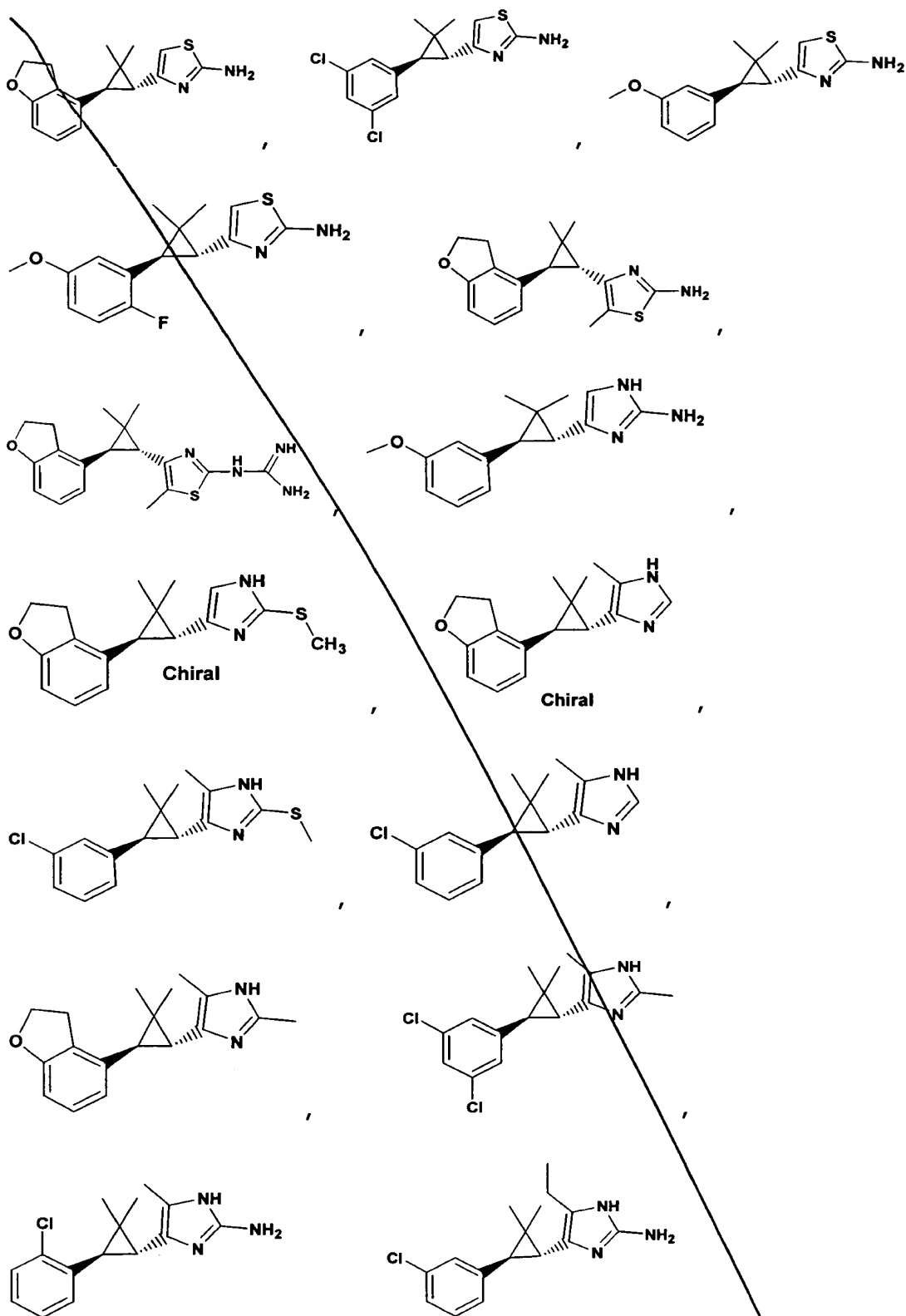
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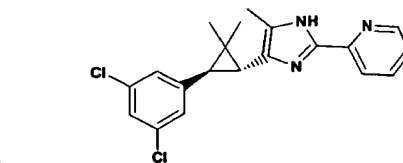
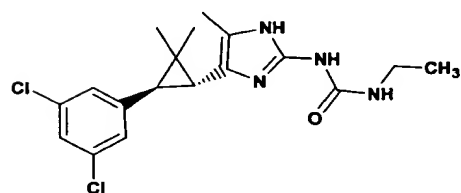
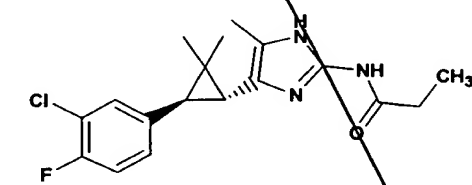
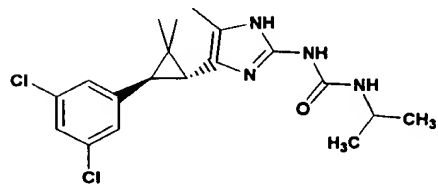
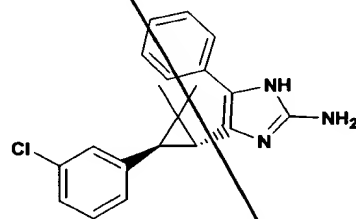
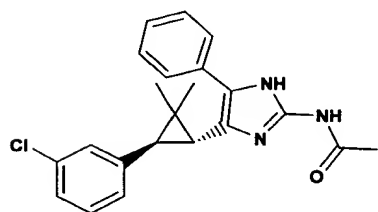
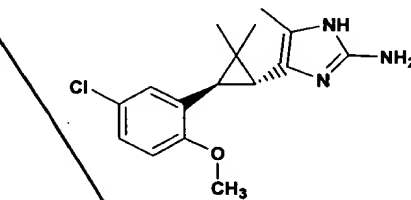
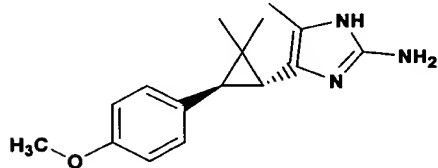
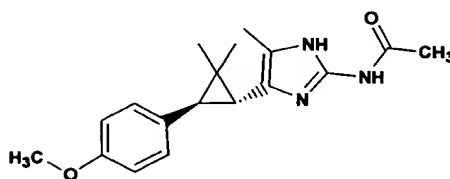
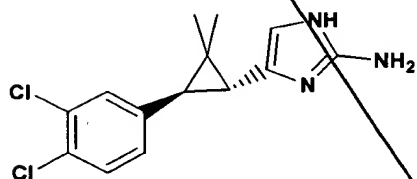
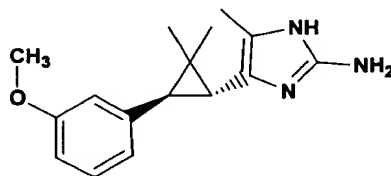
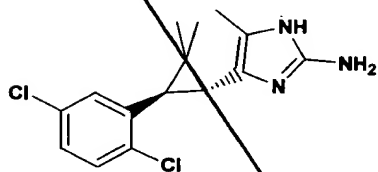
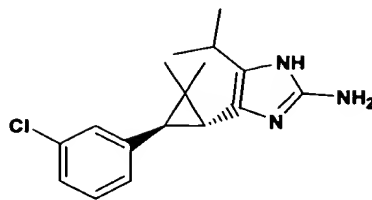
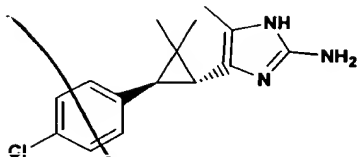


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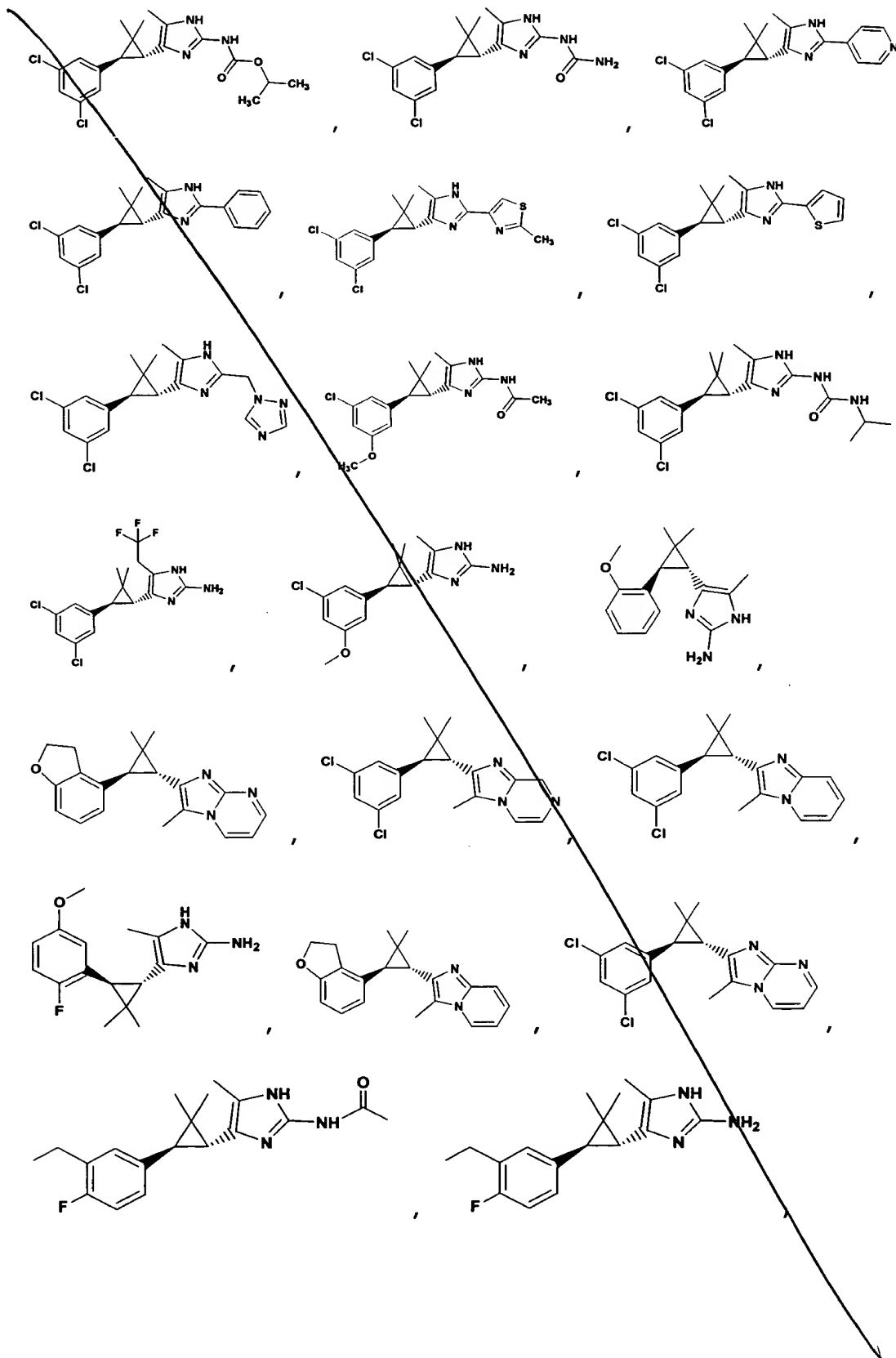


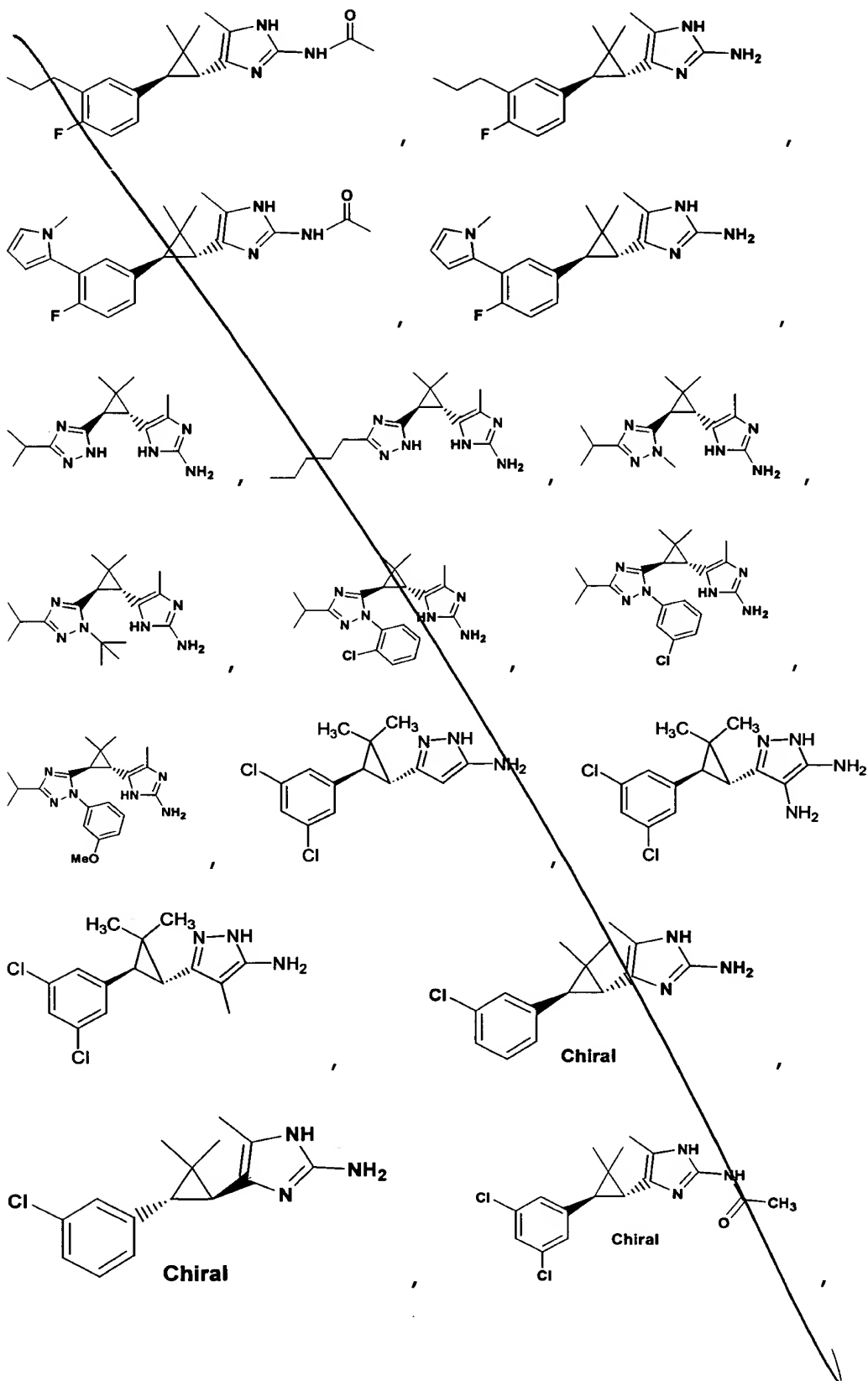
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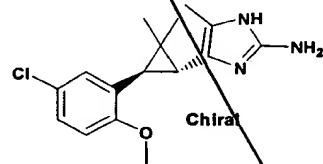
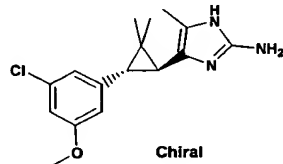
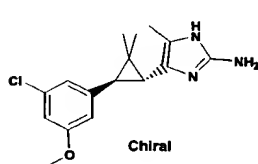
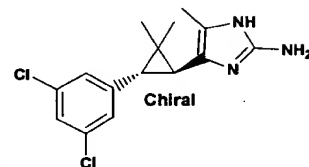
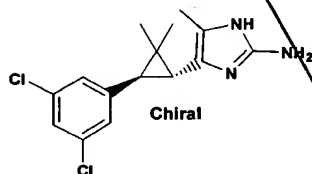
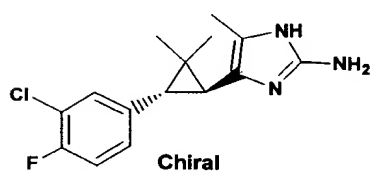
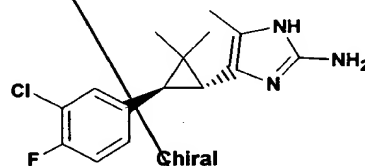
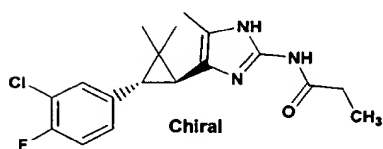
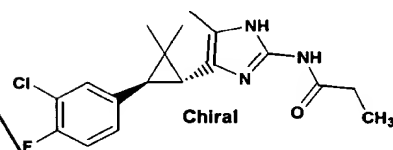
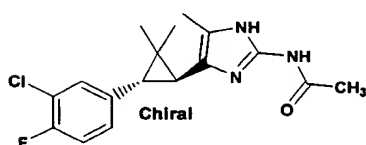
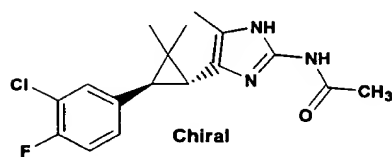
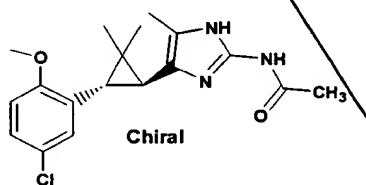
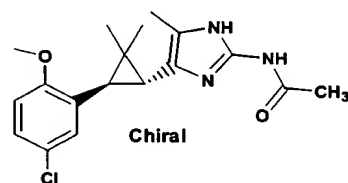
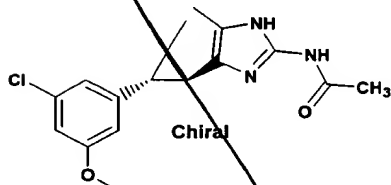
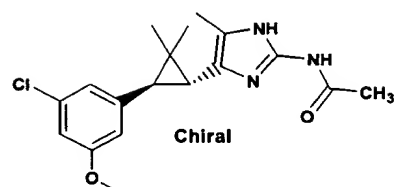
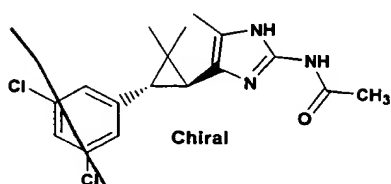
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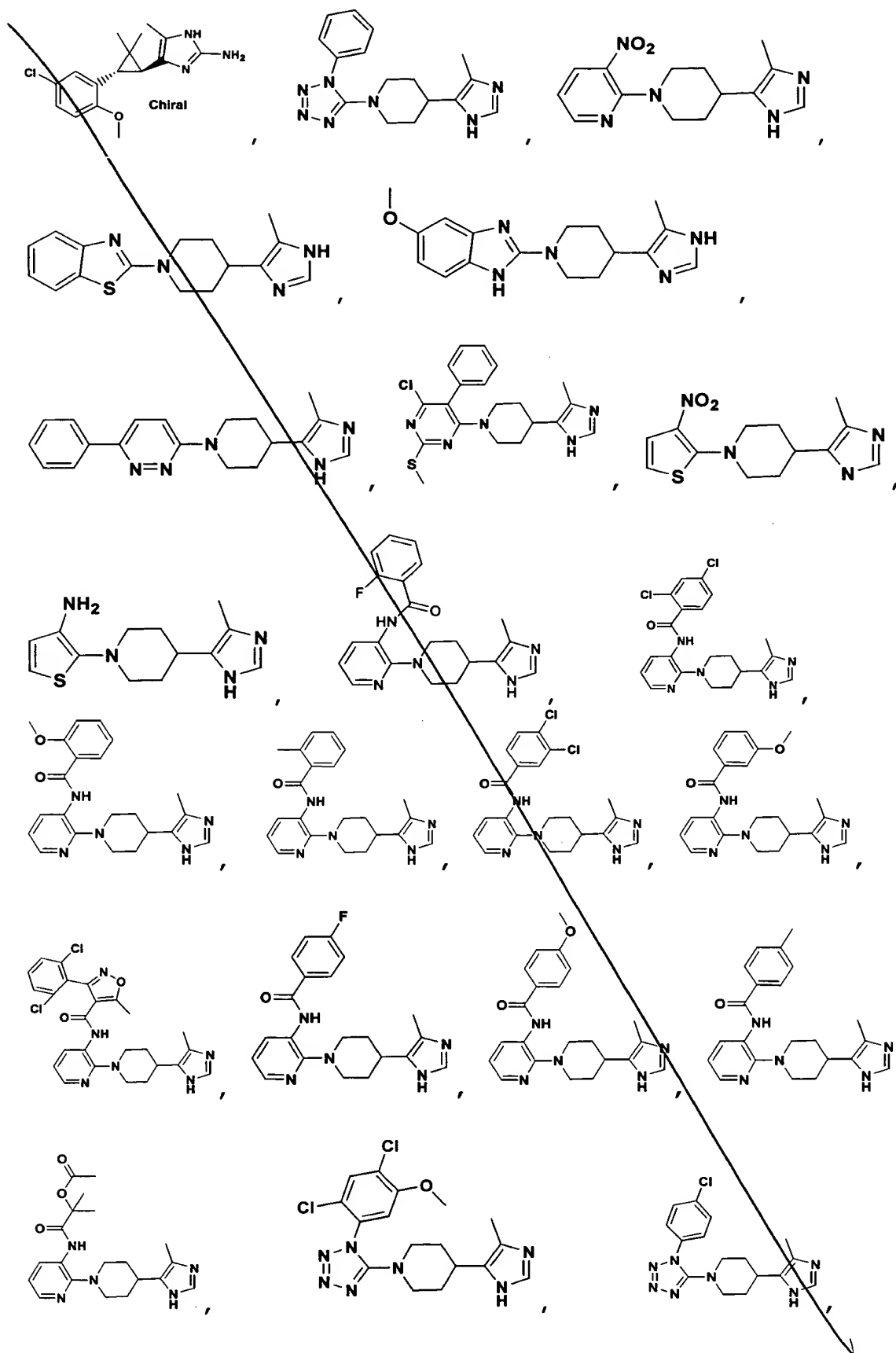
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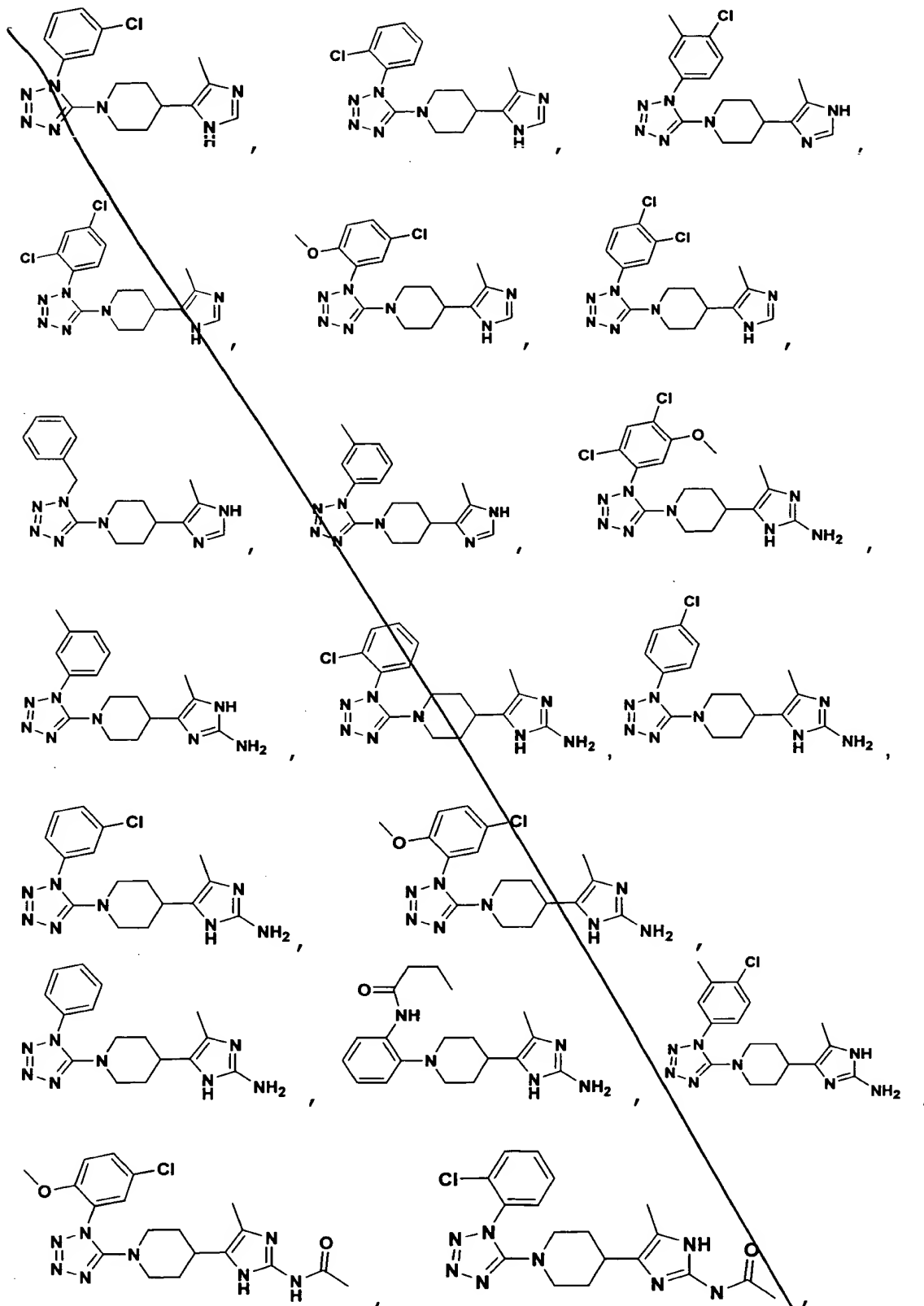
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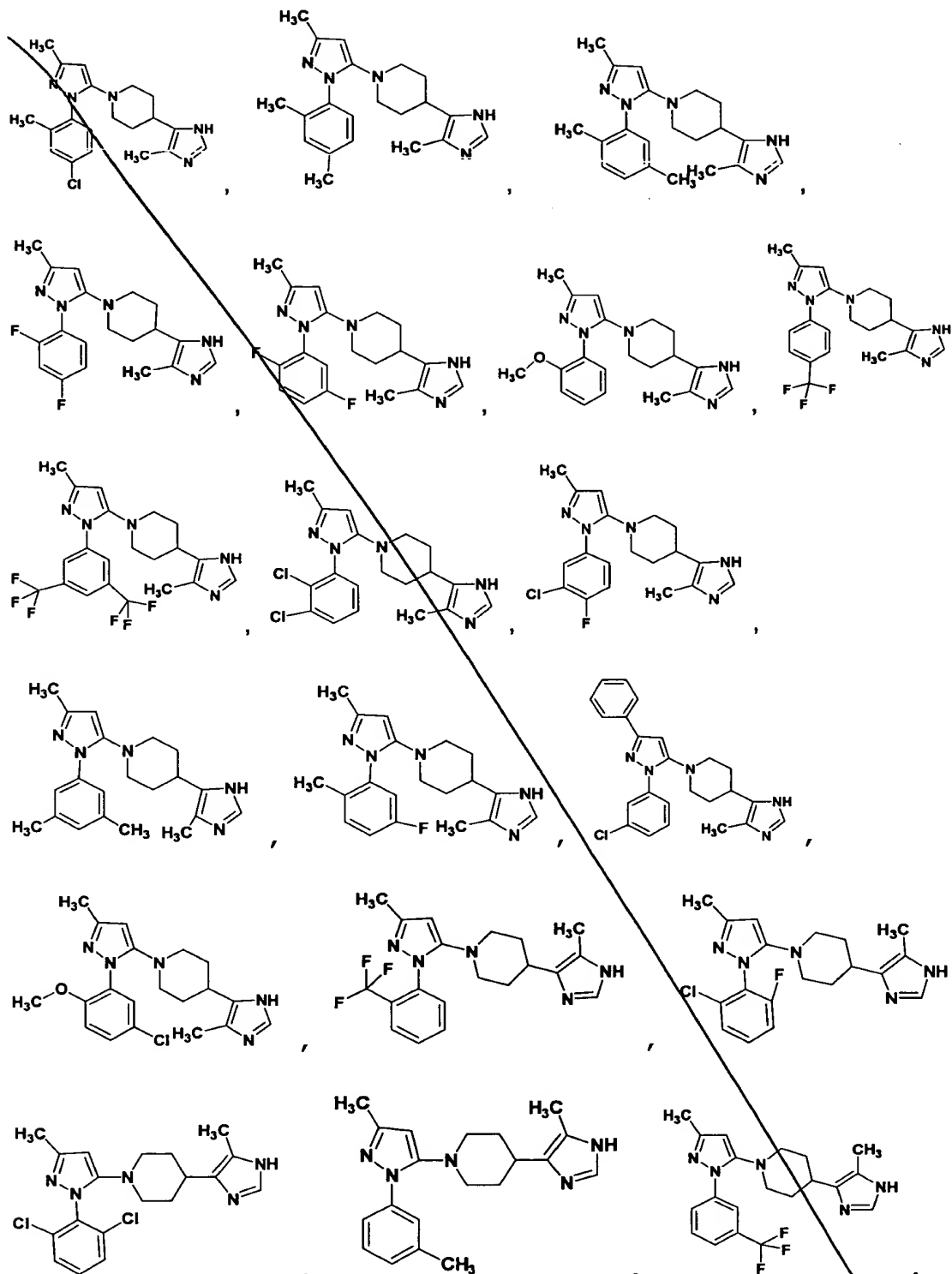


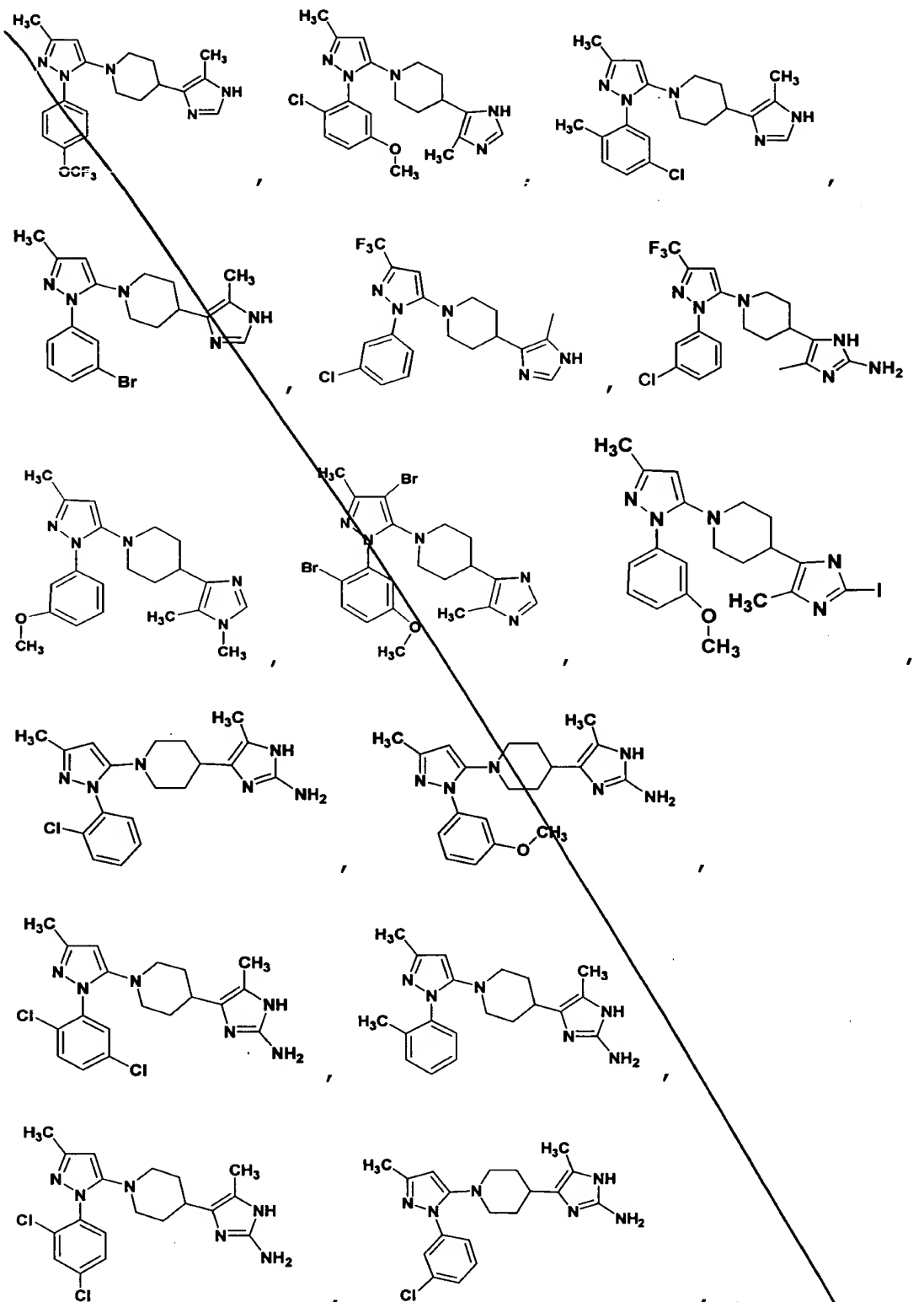
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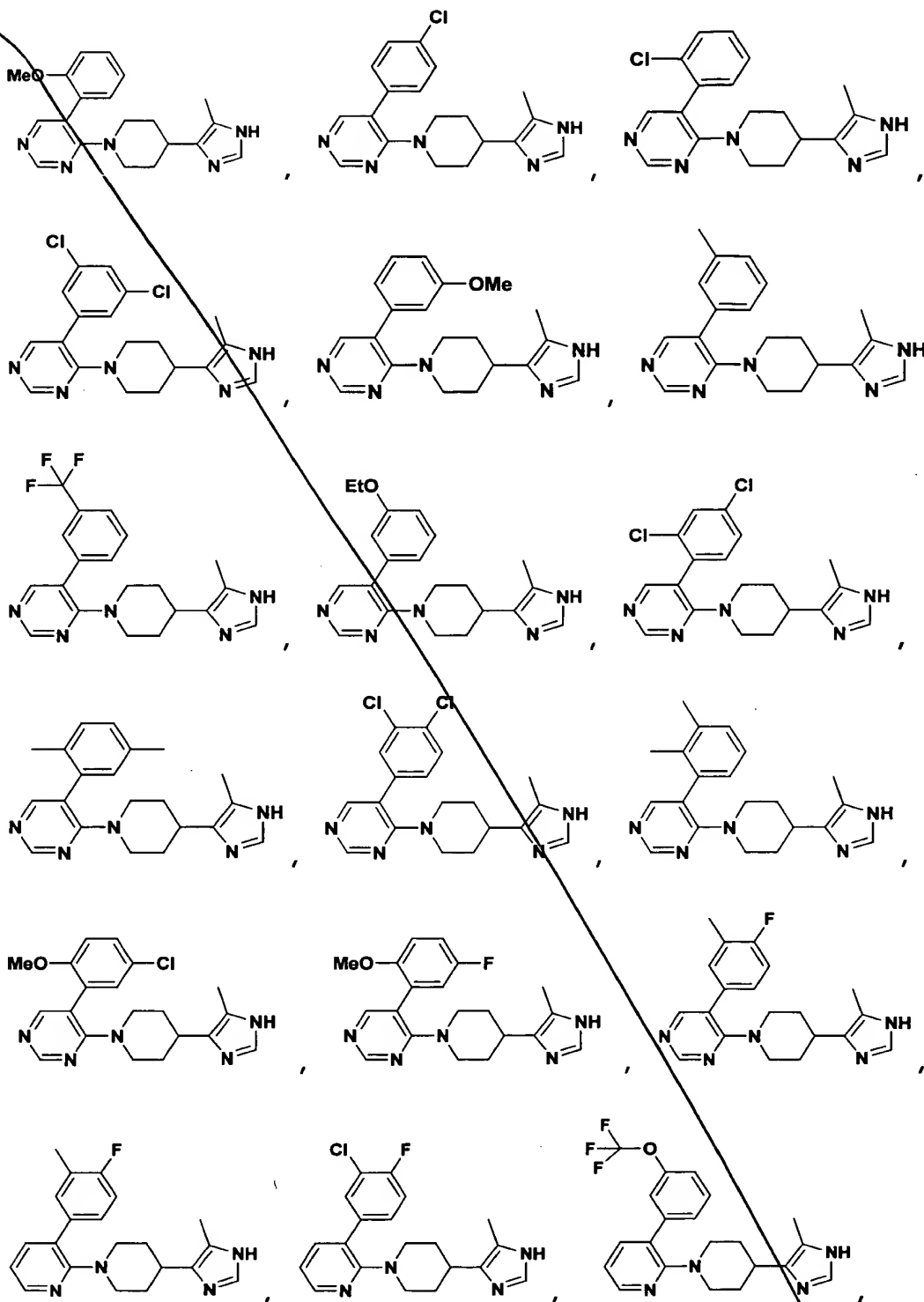


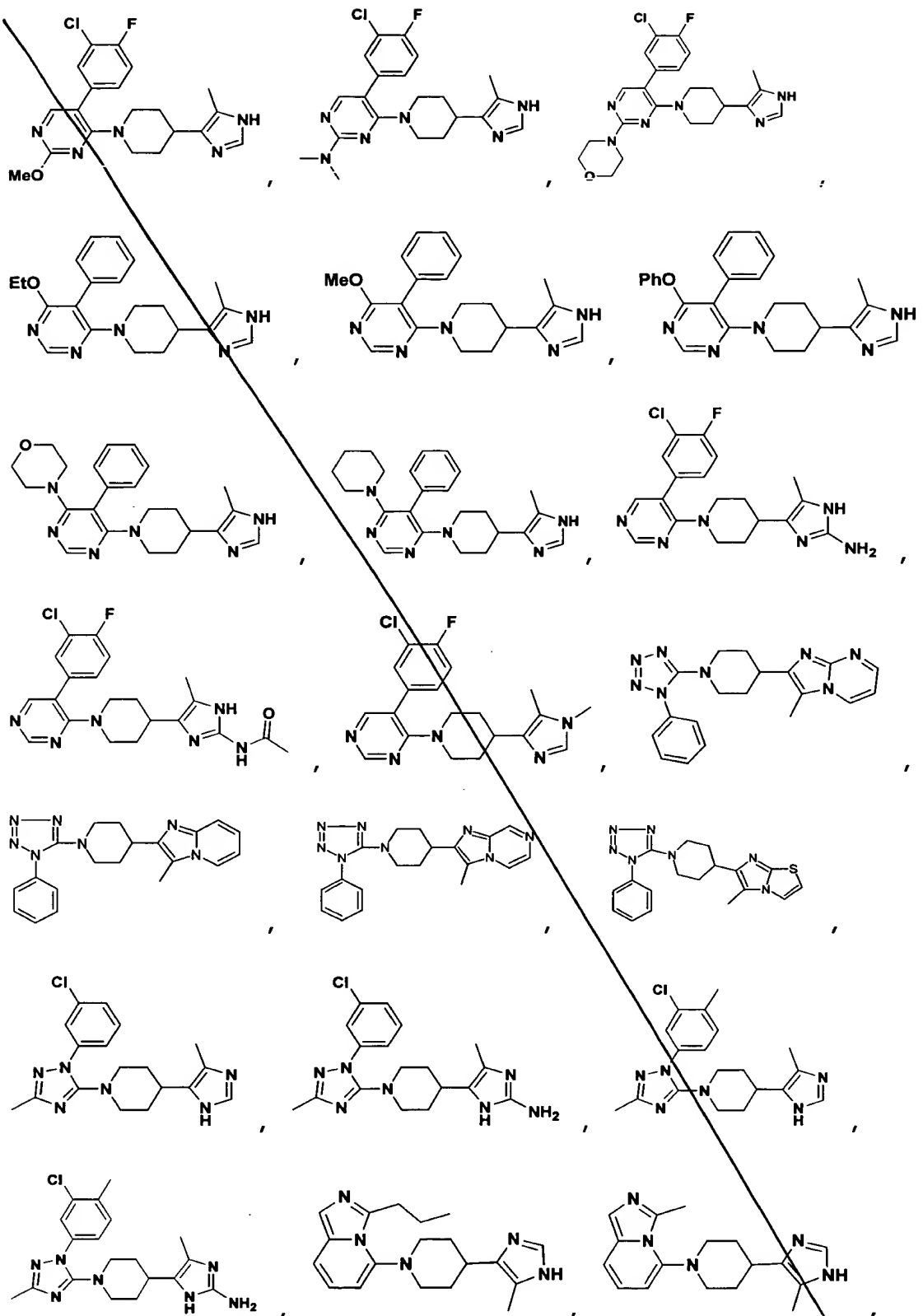
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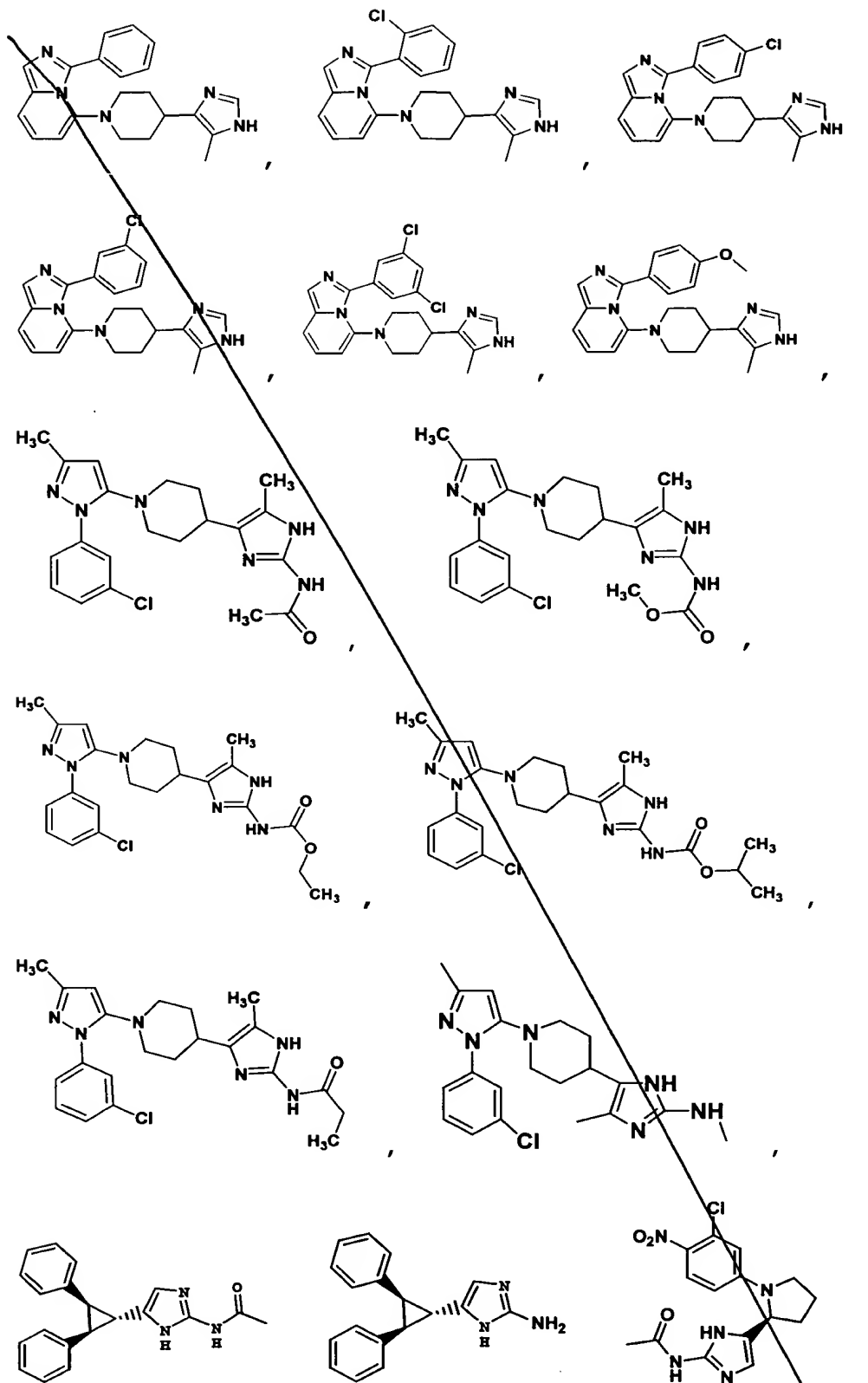
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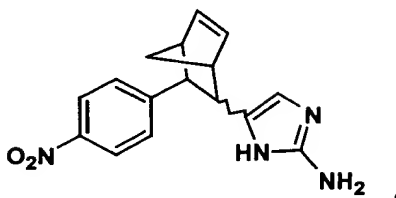
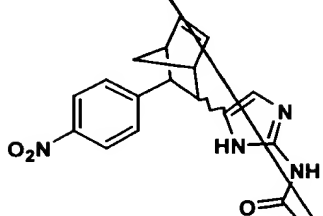
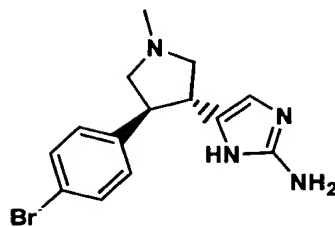
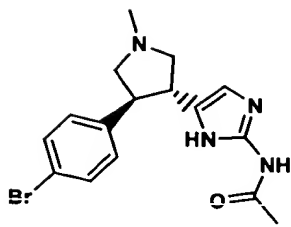
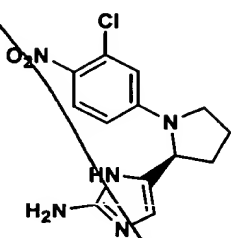


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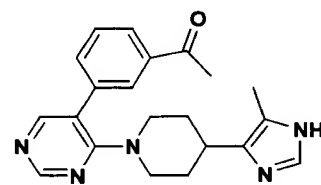
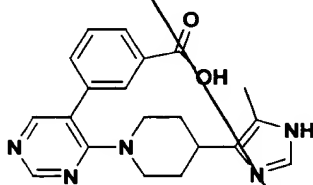
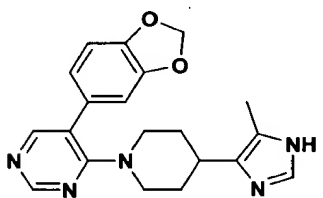
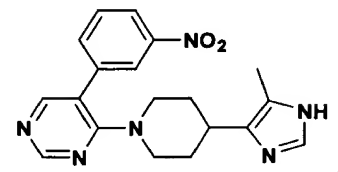
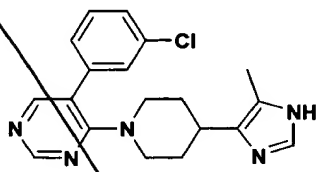
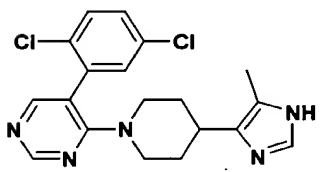


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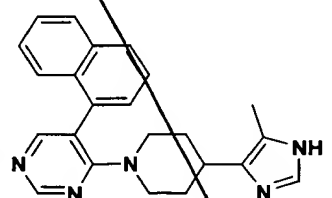
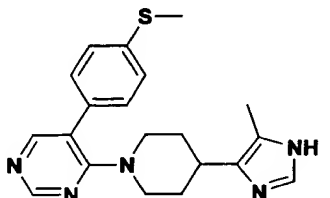
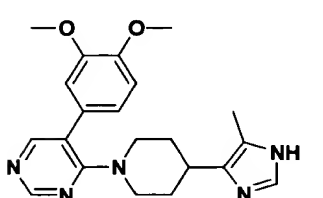
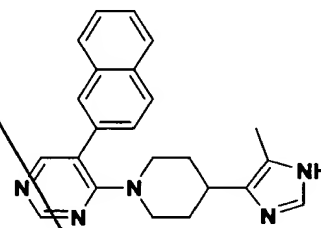
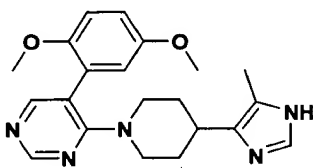
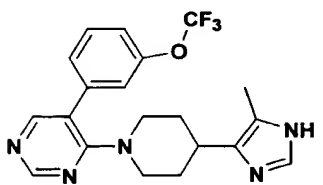
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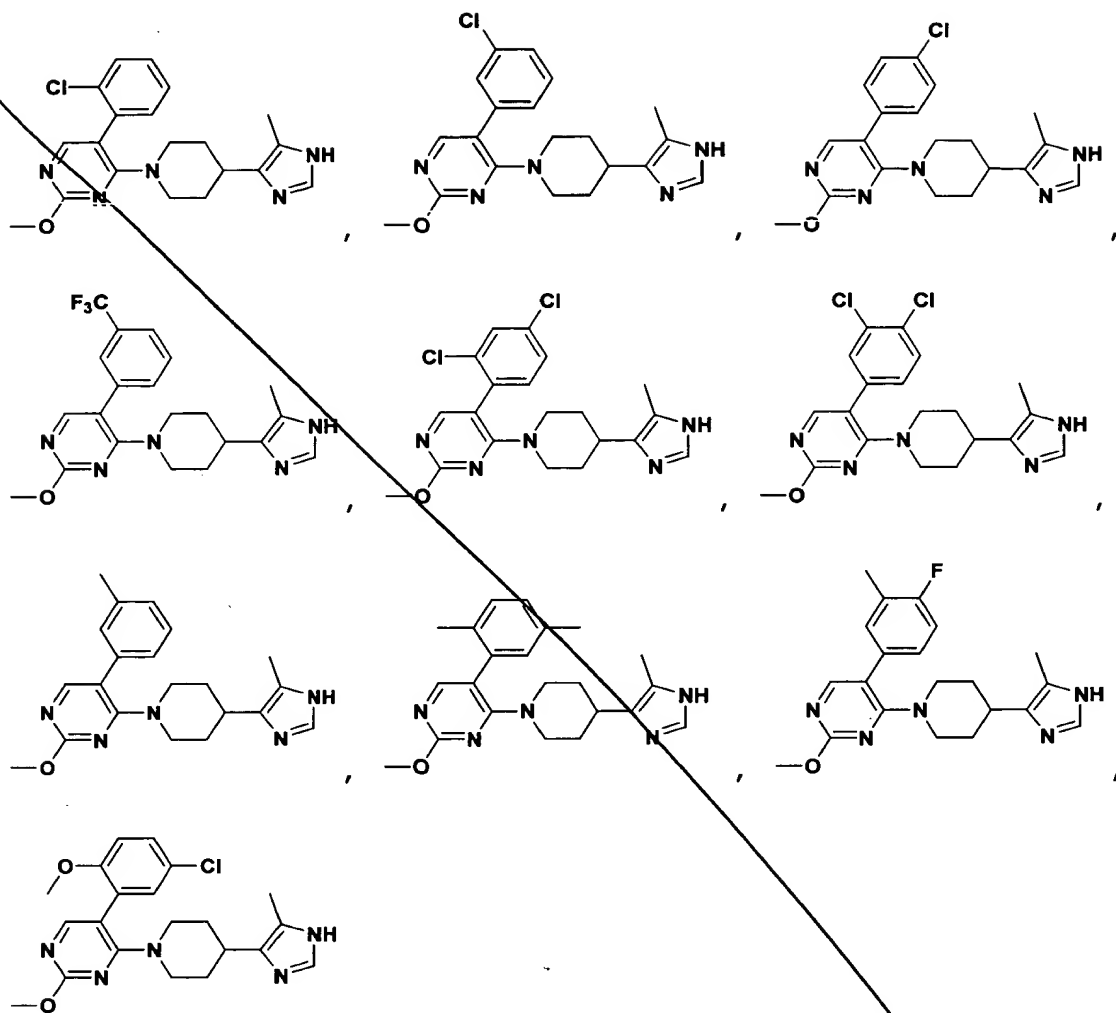
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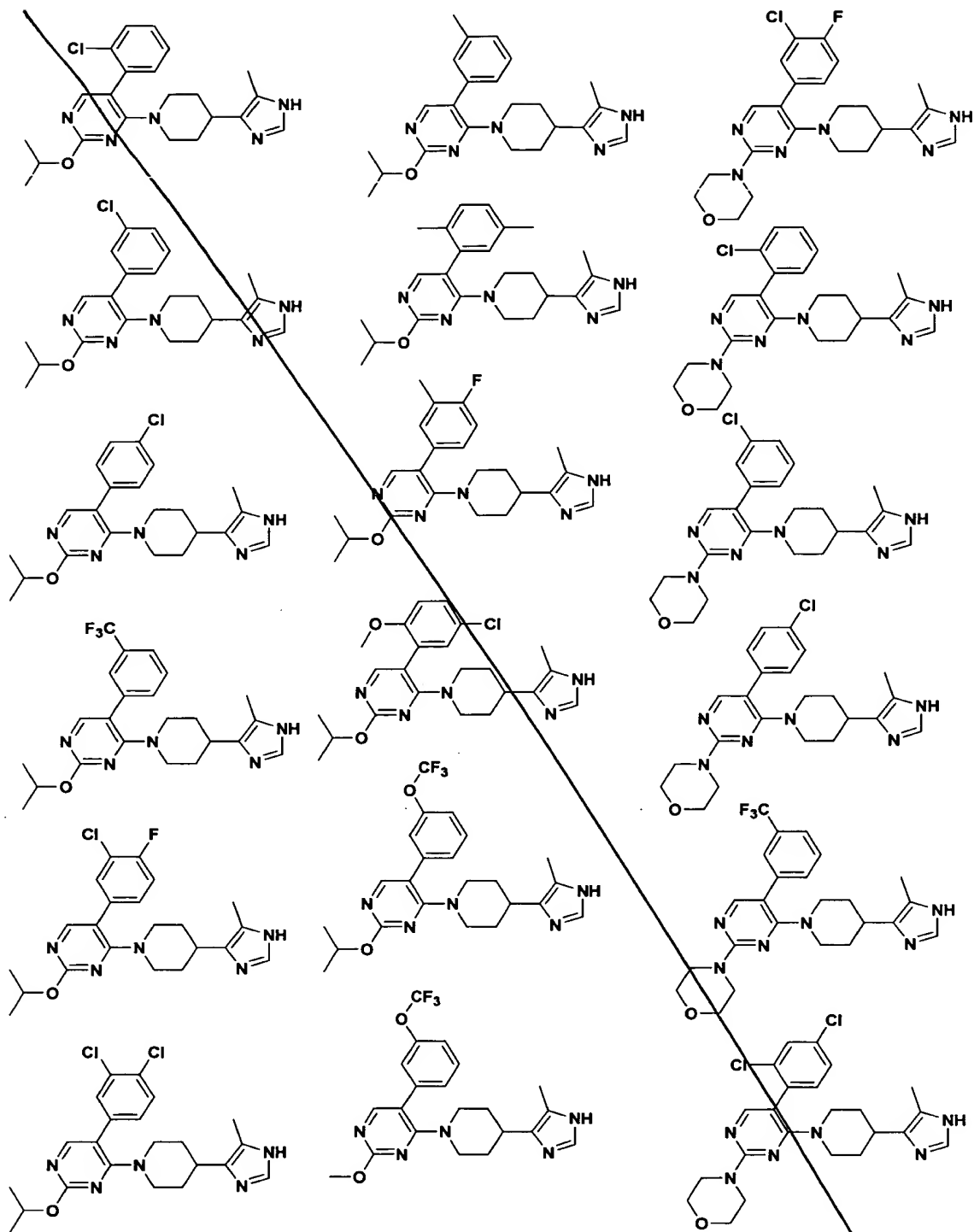


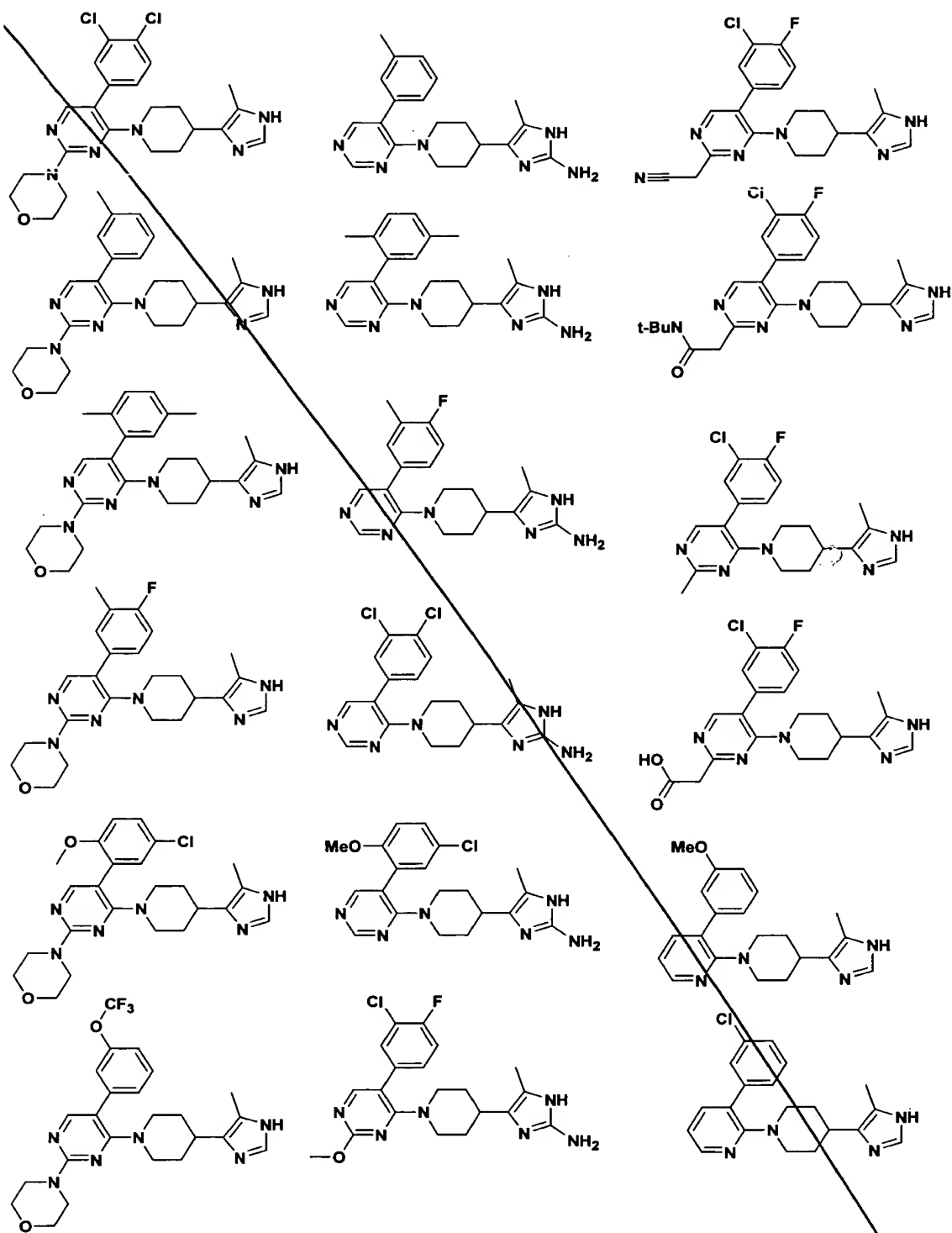




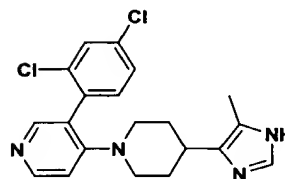
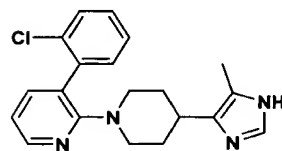
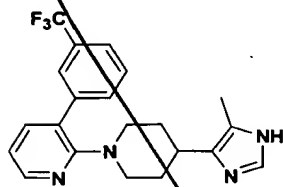
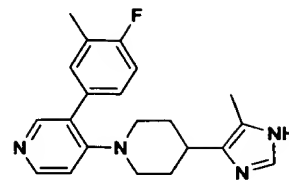
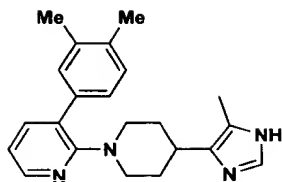
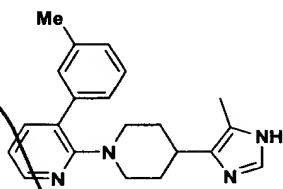
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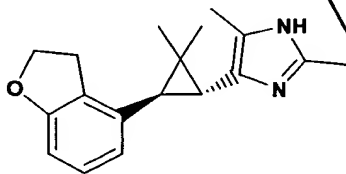
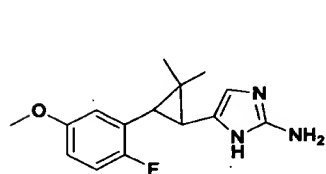
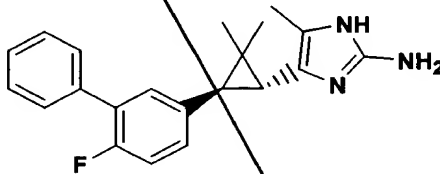
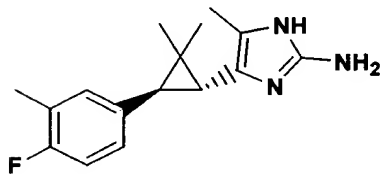
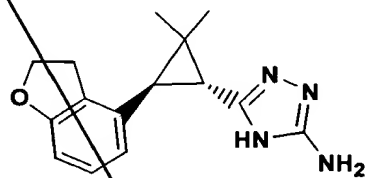
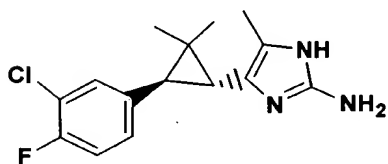
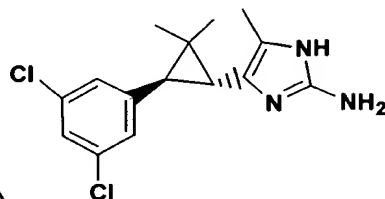
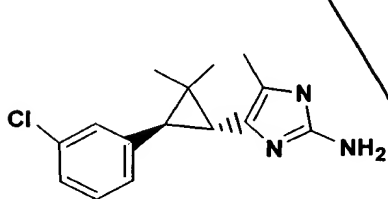


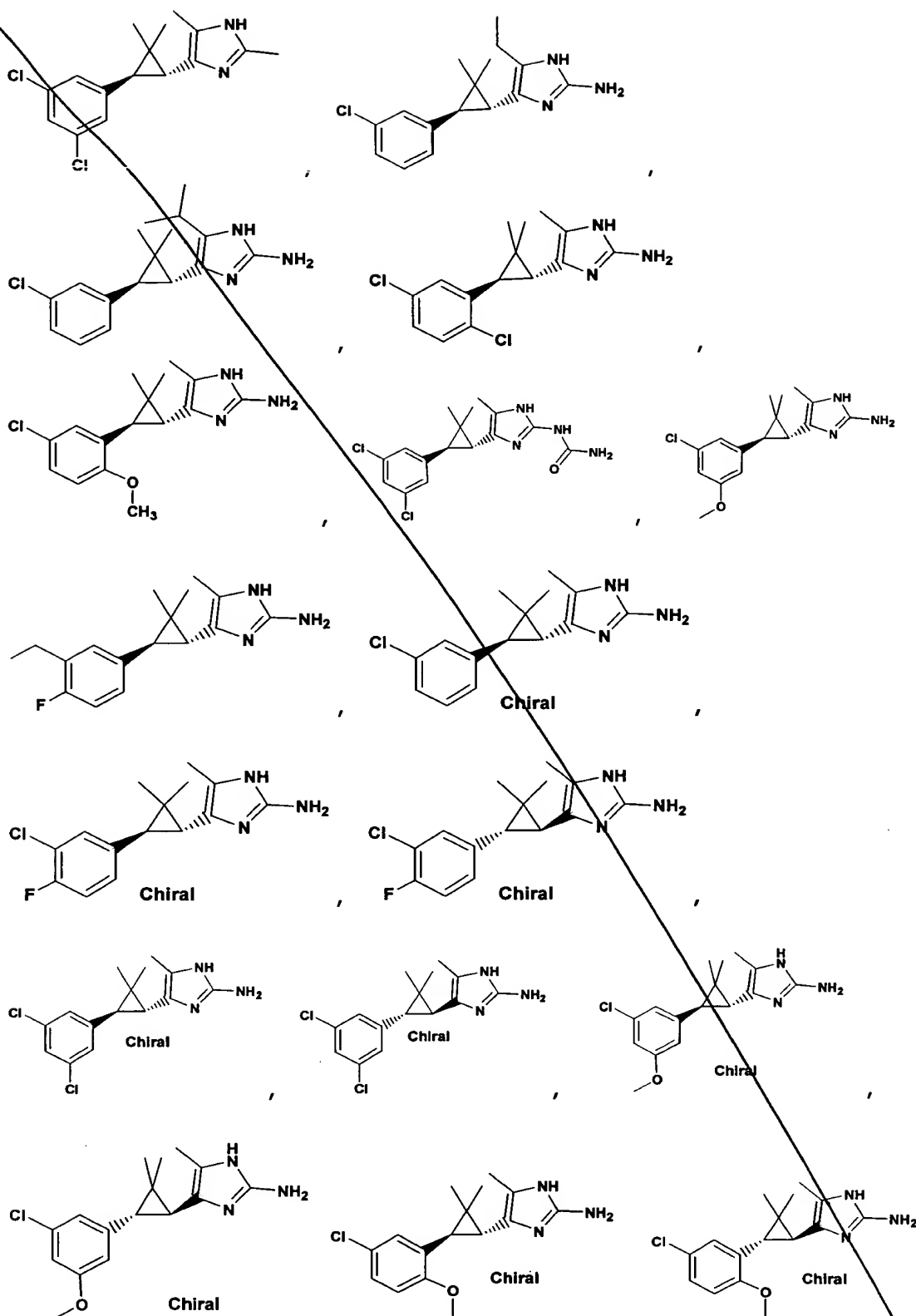
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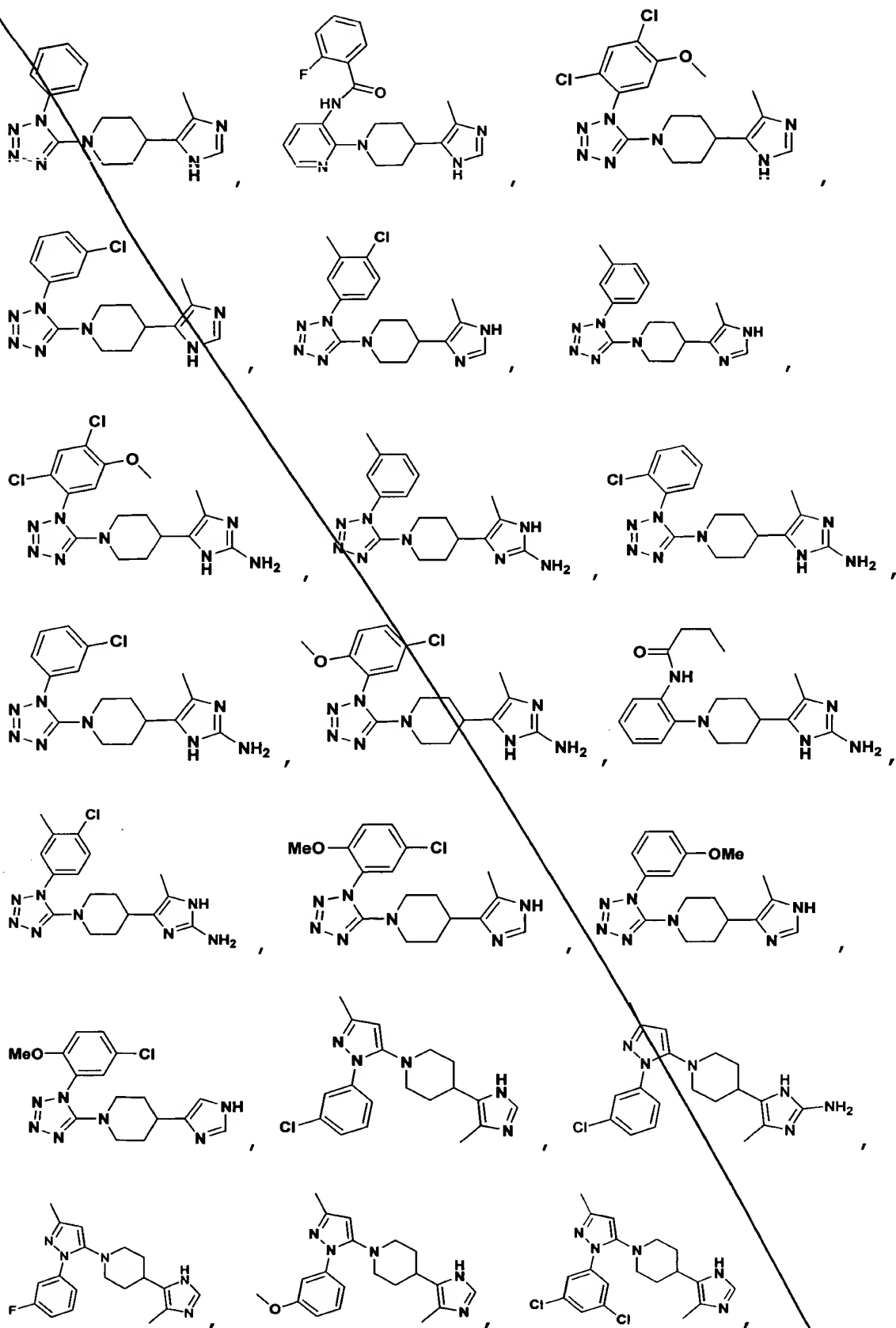


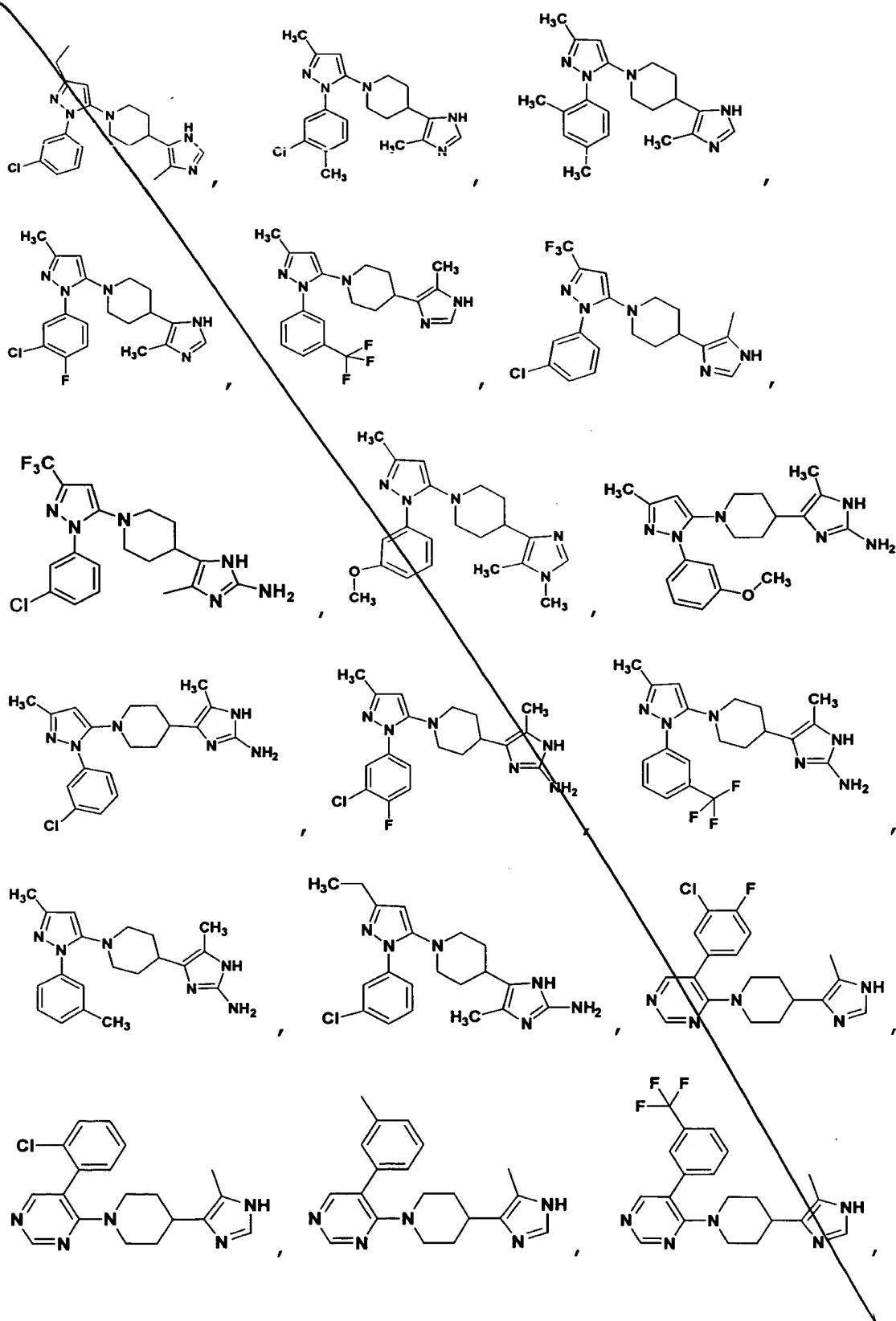
29. The compounds as defined in Claim 1 having the structure



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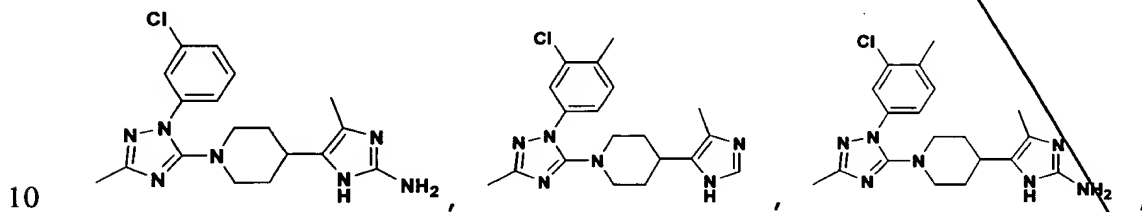
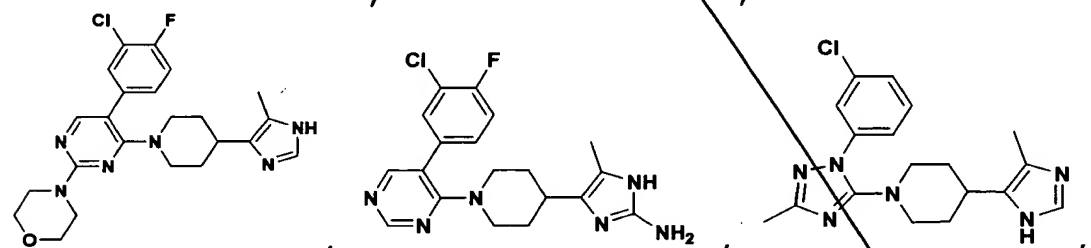
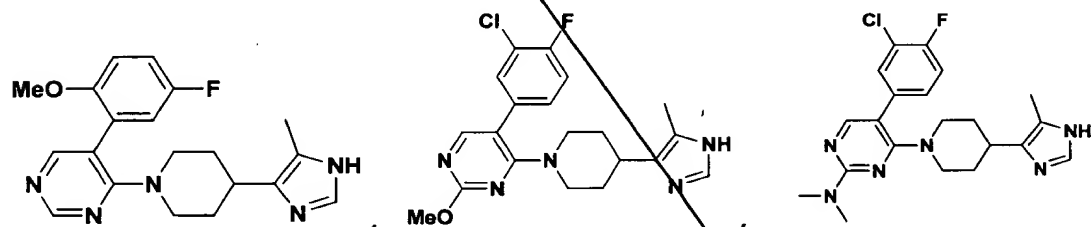
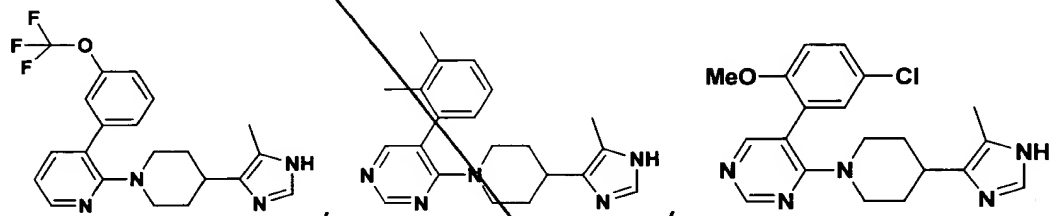
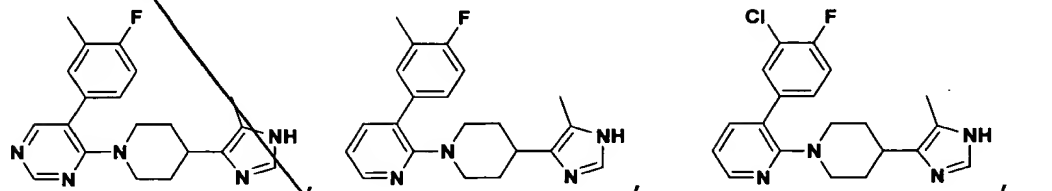
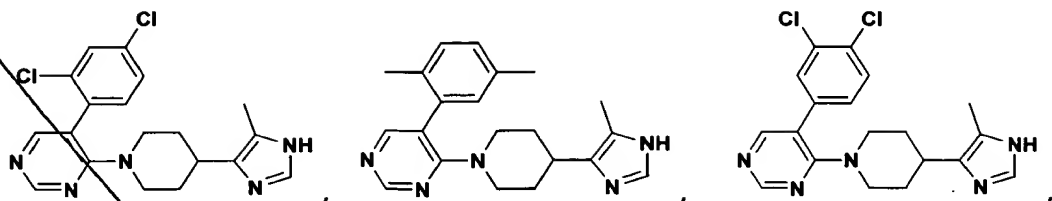
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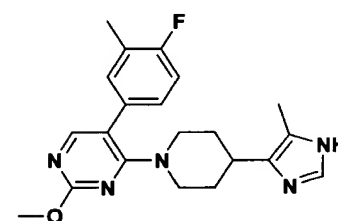
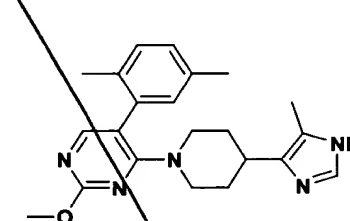
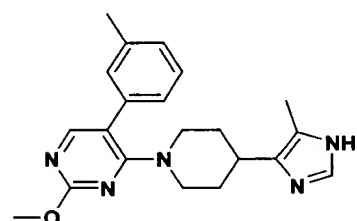
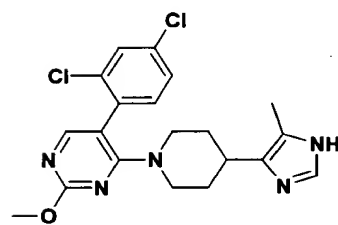
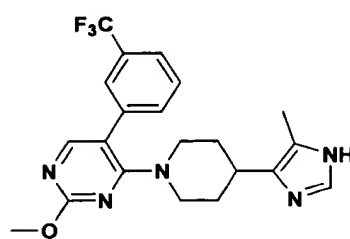
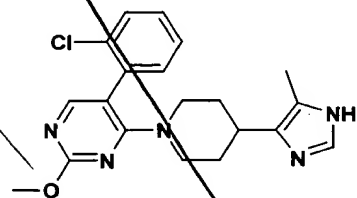
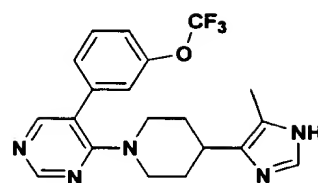
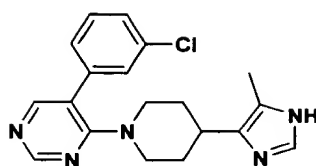
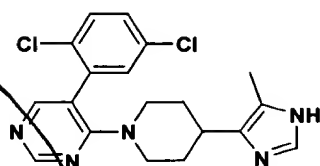


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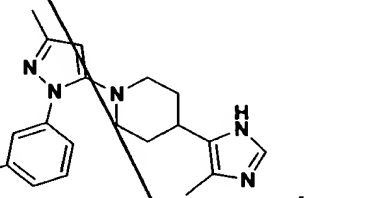
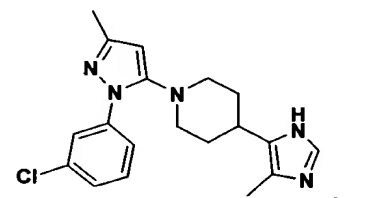
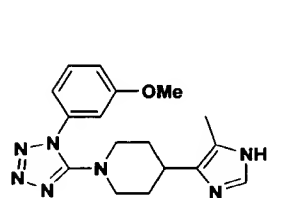
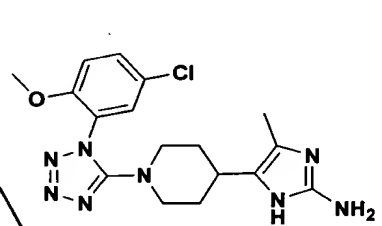
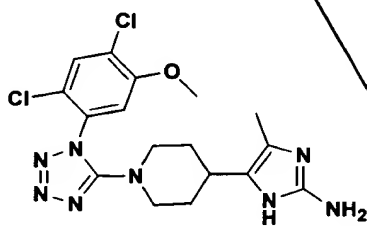
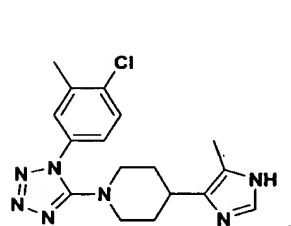
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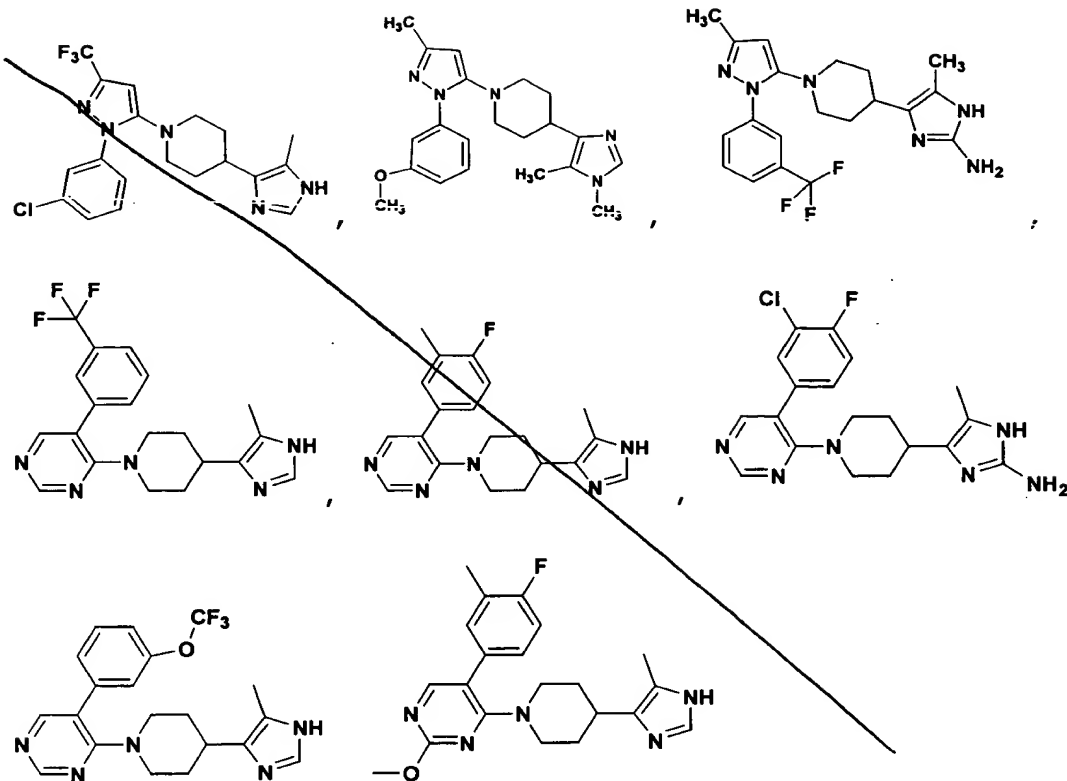
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30. The compound as defined in Claim 1 having the structure







31. A pharmaceutical composition comprising a compound as defined in Claim 1 and a pharmaceutically acceptable carrier therefor

32. A method for preventing or treating disorders caused by intracellular acidosis during myocardial ischemia, hypertension, angina pectoris, cardiac arrhythmia, reperfusion injury, myocardial necrosis, cardiac dysfunction, LDL-cholesterol, renal disease or heart failure, which comprises administering to a mammalian species in need of treatment a therapeutically effective amount of a compound as defined in Claim 1.

33. A method for preventing or treating myocardial ischemia, which comprises administering to a mammalian species in need of treatment a therapeutically effective amount of a compound as defined in Claim 1.

34. A method for preventing or treating an ischemic condition, which comprises administering to a mammalian species in need of treatment a therapeutically

effective amount of an antiischemic agent which is a compound as defined in Claim 1.

35. A method for preventing or treating a peripheral vascular disorder, which comprises  
5 administering to a mammalian species in need of treatment a therapeutically effective amount of an antiischemic agent which is a compound as defined in Claim 1.

36. A method for preventing or treating lower limb ischemia, which comprises administering to a mammalian  
10 species in need of treatment a therapeutically effective amount of an antiischemic agent which is a compound as defined in Claim 1.

37. The method as defined in Claim 34 wherein the peripheral vascular disorder is an ischemic condition.

15 38. The method as defined in Claim 33 wherein the ischemic condition is lower limb ischemia.

39. The method as defined in Claim 33 wherein the ischemic condition is peripheral atherosclerotic disease.

20 40. The method as defined in Claim 38 wherein the peripheral atherosclerotic disease involves intermittent claudication.

41. The method as defined in Claim 34 wherein the peripheral vascular disorder is Raynaud's disease or LeRiches Syndrome.

25 42. A method for the relief of symptoms of pain, paresthesia or discomfort in the lower limb and gluteal regions produced by arterial insufficiency where symptoms are initiated or worsened with ambulation, which comprises administering to a mammalian species in need of  
30 treatment a therapeutically effective amount of a compound as defined in Claim 1.

43. A method for preventing or treating intermittent claudication, which comprises administering to a patient in need of treatment a therapeutically  
35 effective amount of a compound as defined in Claim 1.

44. A pharmaceutical combination comprising a compound as defined in Claim 1 in combination with tissue plasminogen activator (natural or recombinant), streptokinase, reteplase, activase, lanoteplase, urokinase, prourokinase, anisolated streptokinase plasminogen activator complex (ASPAC), or animal salivary gland plasminogen activators.

45. A pharmaceutical combination comprising a compound as defined in Claim 1 in combination with a platelet aggregation inhibitor, an inhibitor of  $\alpha$ -2-antiplasmin, a thromboxane receptor antagonist, a prostacyclin mimetic, a phosphodiesterase (PDE) inhibitor, a thromboxane A synthetase inhibitor, a serotonin-2-receptor antagonist, a fibrinogen receptor antagonist, aspirin, a hypolipidemic agent, an antidiabetic agent, an antihypertensive agent, a  $\beta$ -adrenergic agonist, an anticholinergic agent, an anti-inflammatory corticosteroid or an anti-inflammatory agent or an anti-arrhythmic agent and/or an antiosteoporosis agent.

46. The pharmaceutical combination as defined in Claim 45 wherein the platelet aggregation inhibitor is clopidogrel, ticlopidine, or CS-747, or ifetroban or aspirin.

47. The pharmaceutical combination as defined in Claim 45 wherein the antihypertensive agent is omapatrilat, gemopatrilat, lisinopril, fosinopril, irbesartan, losartan, valsartan, carvedilol or amlodipine besylate.

48. The pharmaceutical combination as defined in Claim 45 wherein the  $\beta$ -adrenergic agonist is albuterol, terbutaline, formoterol, fenoterol, salmeterol, bitolterol, or pilbuterol, and the anti-inflammatory agent is beclomethasone, triamcinolone, flurisolide, dexamethasone, budesonide, fluticasone, cromolyn, nedocromil, theophylline, zileuton, zafirleukast, monteleukast and pranleukast.

49. The pharmaceutical combination as defined in Claim 45 wherein the hypolipodemic agent is pravastatin, simvastatin, atorvastatin, fluvastatin, cerivastatin, AZ4522 or itavastatin.

5 50. A pharmaceutical combination comprising a compound as defined in Claim 1 and a lipid-lowering agent, an antidiabetic agent, an anti-obesity agent, an antihypertensive agent, a platelet aggregation inhibitor, and/or an antiosteoporosis agent.

10 51. The pharmaceutical combination as defined in Claim 50 comprising said compound and an antidiabetic agent.

15 52. The combination as defined in Claim 51 wherein the antidiabetic agent is 1, 2, 3 or more of a biguanide, a sulfonyl urea, a glucosidase inhibitor, a PPAR  $\gamma$  agonist, a PPAR  $\alpha/\gamma$  dual agonist, an SGLT2 inhibitor, a DP4 inhibitor, an  $\alpha$ P2 inhibitor, an insulin sensitizer, a glucagon-like peptide-1 (GLP-1), insulin and/or a meglitinide.

20 53. The combination as defined in Claim 52 wherein the antidiabetic agent is 1, 2, 3 or more of metformin, glyburide, glimepiride, glipyrizide, glipizide, chlorpropamide, gliclazide, acarbose, miglitol, pioglitazone, troglitazone, rosiglitazone, insulin, Gl-  
25 262570, isaglitazone, JTT-501, NN-2344, L895645, YM-440, R-119702, AJ9677, repaglinide, nateglinide, KAD1129, AR-HO39242, GW-409544, KRP297, AC2993, LY315902, P32/98 and/or NVP-DPP-728A.

30 54. The combination as defined in Claim 52 wherein the compound is present in a weight ratio to the antidiabetic agent within the range from about 0.001 to about 100:1.

35 55. The combination as defined in Claim 51 wherein the anti-obesity agent is a beta 3 adrenergic agonist, a lipase inhibitor, a serotonin (and dopamine) reuptake inhibitor, a thyroid receptor beta compound, an  $\alpha$ P2 inhibitor and/or an anorectic agent.

56. The combination as defined in Claim 55 wherein the anti-obesity agent is orlistat, ATL-962, AJ9677, L750355, CP331648, sibutramine, topiramate, axokine, dexamphetamine, phentermine, phenylpropanolamine, and/or mazindol.

57. The combination as defined in Claim 51 wherein the lipid lowering agent is an MTP inhibitor, an HMG CoA reductase inhibitor, a squalene synthetase inhibitor, a fibric acid derivative, an upregulator of LDL receptor activity, a lipoxxygenase inhibitor, or an ACAT inhibitor.

58. The combination as defined in Claim 57 wherein the lipid lowering agent is pravastatin, lovastatin, simvastatin, atorvastatin, cerivastatin, fluvastatin, itavastatin, visastatin, fenofibrate, gemfibrozil, clofibrate, avasimibe, TS-962, MD-700, cholestagel, niacin and/or LY295427.

59. The combination as defined in Claim 57 wherein the compound is present in a weight ratio to the lipid-lowering agent within the range from about 0.001:1 to about 100:1.

60. The combination as defined in Claim 50 wherein the antihypertensive agent is an ACE inhibitor, angiotensin II receptor antagonist, NEP/ACE inhibitor, calcium channel blocker and/or  $\beta$ -adrenergic blocker.

61. The combination as defined in Claim 60 wherein the antihypertensive agent is an ACE inhibitor which is captopril, fosinopril, enalapril, lisinopril, quinapril, benazepril, fentiapril, ramipril or moexipril;

an NEP/ACE inhibitor which is omapatrilat, [S[(R\*,R\*)]-hexahydro-6-[(2-mercapto-1-oxo-3-phenylpropyl)amino]-2,2-dimethyl-7-oxo-1H-azepine-1-acetic acid (gemopatrilat) or CGS 30440;

an angiotensin II receptor antagonist which is irbesartan, losartan or valsartan;

amlodipine besylate, prazosin HCl, verapamil, nifedipine, nadolol, propranolol, carvedilol, or clonidine HCl.

62. The combination as defined in Claim 50 wherein the platelet aggregation inhibitor is aspirin, clopidogrel, ticlopidine, dipyridamole or ifetroban.

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